

Associations of Lifestyle with Physical and Mental Health in Switzerland

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von

Aline Richard

von Oberegg AI

Promotionskomitee

PD Dr. Sabine Rohrmann (Vorsitz)

Prof. Milo Puhan

Prof. Martin Preisig

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Table of Contents

SUMMARY	4
ZUSAMMENFASSUNG	7
INTRODUCTION	11
THE PUBLIC HEALTH RELEVANCE AND EPIDEMIOLOGY OF LIFESTYLE AND HEALTH	12
LIFESTYLE AND HEALTH IN SWITZERLAND	16
DATA COLLECTION IN SWITZERLAND	17
AIMS OF THE THESIS	18
CONTRIBUTIONS OF THE THESIS DEFENDANT TO THE WORK PRESENTED	23
CHAPTER 1	30
ASSOCIATIONS BETWEEN FRUIT AND VEGETABLE CONSUMPTION AND PSYCHOLOGICAL DISTRESS:	
RESULTS FROM A POPULATION-BASED STUDY	31
CHAPTER 2	51
IS BODY WEIGHT DISSATISFACTION A PREDICTOR OF DEPRESSION INDEPENDENT OF BODY MASS INDEX,	
SEX AND AGE? RESULTS OF A CROSS-SECTIONAL STUDY	52
CHAPTER 3	72
LONELINESS IS ADVERSELY ASSOCIATED WITH LIFESTYLE AND PHYSICAL AND MENTAL HEALTH.	
RESULTS OF A CROSS-SECTIONAL STUDY FROM SWITZERLAND	73
CHAPTER 4	98
LIFESTYLE AND HEALTH-RELATED PREDICTORS OF CERVICAL CANCER SCREENING ATTENDANCE	
IN A SWISS POPULATION-BASED STUDY	99
CHAPTER 5	120
PREVALENCE OF VITAMIN D DEFICIENCY AND ITS ASSOCIATIONS WITH SKIN COLOR IN PREGNANT	
WOMEN IN THE FIRST TRIMESTER IN A SAMPLE FROM SWITZERLAND	121
SUMMARY AND CONCLUSIONS	140

Summary

Health is not only understood as the absence of illness but as a state of complete physical, mental and social well-being (World Health Organization). Thus, health of an individual does not only depend on its biological and genetic predispositions, but also on the social, cultural and ecological environment, and on lifestyle, behavior and the services of the health care system.

Impaired health manifests itself in morbidity or even premature mortality. Therefore, it is a major public health concern to assess the prevalence rates of diseases and health related factors, and to evaluate how the risk of morbidity and mortality can be diminished. Among all diseases non-communicable diseases (NCD) account for more than 85% of the global burden of disease. NCDs are in general chronic diseases of long duration and slow progression.

In Switzerland, data collection on a national level about lifestyle and health of individuals living in Switzerland is limited and associations of lifestyle with health are insufficiently studied. This is particularly true for mental health, which has been less consistently examined compared with other NCDs. The majority of premature NCD deaths are preventable and, thus, of great public health relevance.

In this thesis, a focus was set on modifiable lifestyle and health-related factors and their associations with NCDs, including mental diseases (chapter 1 to 4) for individuals living in Switzerland. Additionally, aspects of nutritional deficiency were emphasized in chapter 5.

For this thesis, data mainly from the population-based Swiss Health Survey 2012 were used to provide new information about a variety of so far unknown prevalence rates of health-related factors and about potential associations between health and lifestyle for the population living in Switzerland. The examined associations in the 5 chapters of the thesis are presented as follows:

Chapter 1: Diet is one of the most important modifiable factors that affect health in various ways. Thus, associations of the adherence to the 5-a-day-recommendations of fruit and vegetable consumption with psychological distress were examined. Results indicate that keeping to the 5-a-day recommendation was associated with lower psychological distress in Switzerland.

Chapter 2: A variety of intrapersonal factors influence the own satisfaction about one's life or single aspects of life, such as feelings, attitudes, perceptions, and behaviors and thus, can affect health, including mental health. The aim was to examine if body weight dissatisfaction (BWD) is a risk factor for depression. In this analysis, BWD was widespread, affecting nearly one fourth of the population living in Switzerland. Furthermore, BWD was associated with depression, independent of age, sex, and body mass index.

Chapter 3: Not only manifest psychiatric disorders but also possible precursors, such as loneliness, are common in the population and may be associated with unhealthy lifestyle and physical and mental illness. Hence, the associations of loneliness with lifestyle, physical and mental health were studied. Loneliness was apparent throughout the total age range of adulthood and was associated with unhealthy behavior, such as smoking or insufficient physical activity, and poorer physical and mental health in Switzerland.

Chapter 4: Healthy lifestyles are not only related to health directly but also to health behaviors, e.g. to participation in screenings. Thus, in this chapter, the associations of healthy lifestyle with participation to cervical cancer screening were assessed. Results indicate that being obese, physically inactive and non-attention to diet are risk factors for cervical cancer screening attendance in Switzerland.

Chapter 5: Genetic predispositions also have an impact on health, such as skin color on vitamin D status. The main source of vitamin D is sunlight (UVB) which is required for vitamin D production in the skin. This production depends on skin color. By collecting data from 204 pregnant women in the University Hospital of Zurich the prevalence of serum vitamin D deficiency (< 20 ng/mL) and the association of skin color with vitamin D deficiency were evaluated. Almost two third of all women were vitamin D deficient and the likelihood of vitamin D deficiency was higher in dark-skinned women compared to women with light skin color.

This thesis assessed several so far unknown prevalence rates for a variety of health related factors in Switzerland, and examined associations between lifestyle and health in Switzerland. Results from this thesis indicate that lifestyle and health are strongly linked; lifestyle changes – e.g. the adherence to the 5-a-day recommendation – can have a positive effect on health. In relation to an undesirable emotional state, such as loneliness, it may be worthwhile to achieve changes before a manifest psychiatric disorder or physical illness

develops. In the face of the aging population and resulting rising NCDs it makes sense to target a healthy lifestyle for the benefit of physical and mental health. However, due to the cross-sectional design, results of the present thesis have to be confirmed in future longitudinal population-based cohort studies.

Zusammenfassung

Gesundheit wird nicht nur als die Abwesenheit von Krankheit verstanden sondern als Zustand des vollkommenen körperlichen, seelischen und sozialen Wohlbefindens (Weltgesundheitsorganisation). Somit hängt die Gesundheit des Individuums nicht nur von biologischen und genetischen Prädispositionen ab, sondern auch von der sozialen, kulturellen und ökonomischen Umwelt, vom Lebensstil, vom Verhalten und von der Versorgung des Gesundheitssystems.

Eine eingeschränkte Gesundheit äussert sich in Krankheiten oder sogar in vorzeitigem Tod. Es ist deshalb von öffentlichem Interesse, die Häufigkeiten von Krankheiten zu evaluieren und zu untersuchen, wie das Risiko für Krankheiten und vorzeitigen Tod vermindert werden kann. Unter den Krankheiten machen die nicht-übertragbaren Krankheiten (NCD) mehr als 85% von der gesamten Krankheitslast aus. NCDs sind meist chronische Krankheiten von langer Dauer und gekennzeichnet durch ein langsames Fortschreiten der Krankheit.

In der Schweiz ist die Datensammlung über Gesundheit und Lebensstil auf nationaler Ebene spärlich, und Zusammenhänge zwischen Lebensstil und Gesundheit sind ungenügend erforscht, insbesondere bei psychischen Störungen. Ein Grossteil der Todesfälle aufgrund von NCDs gilt als vermeidbar und ist deshalb von Bedeutung für die öffentliche Gesundheit.

In dieser Arbeit liegt der Schwerpunkt auf modifizierbaren Lebensstil- und gesundheitsbezogenen Faktoren im Zusammenhang mit NCDs - inklusive psychischen Störungen - (Kapitel 1 bis 4) für in der Schweiz lebende Personen. Des Weiteren wird ein Aspekt der Mangelernährung beleuchtet (Kapitel 5).

In dieser Arbeit wurden vorwiegend Daten aus der Schweizerischen Gesundheitsbefragung von 2012 verwendet. Es werden bisher unbekannte Prävalenzen zu gesundheitsbezogenen Faktoren aufgezeigt und Zusammenhänge zwischen Gesundheit und Lebensstil in der Schweiz analysiert. Diese Zusammenhänge werden in dieser Arbeit in 5 Kapiteln dargestellt und im Folgenden kurz zusammengefasst:

Kapitel 1: Ernährung stellt einen wesentlichen veränderbaren Lebensstilfaktor dar, welcher die Gesundheit beeinflussen kann. In diesem Kapitel wurde der Zusammenhang zwischen dem Einhalten der 5-am-Tag Empfehlung zu Früchte- und Gemüsekonsum und psychischer

Belastung untersucht. Die Resultate zeigen, dass das Einhalten der 5-am-Tag Empfehlung in der Schweiz mit besserem psychischem Wohlbefinden verbunden ist.

Kapitel 2: Verschiedene intrapersonelle Faktoren beeinflussen die Zufriedenheit des Einzelnen mit Aspekten des Lebens, wie z.B. Gefühle, Haltungen, Wahrnehmungen und Verhalten. Diese wiederum können die Gesundheit, auch die psychische Gesundheit beeinflussen. Das Ziel dieses Kapitels war es, den Zusammenhang zwischen Zufriedenheit mit dem Körpergewicht und Depression zu analysieren. Insgesamt hat sich gezeigt, dass knapp ein Viertel der Bevölkerung in der Schweiz unzufrieden mit ihrem Körpergewicht ist. Zudem war diese Unzufriedenheit mit Depression verbunden. Dieser Zusammenhang bestand unabhängig von Alter, Geschlecht und Body Mass Index.

Kapitel 3: Nicht nur vorhandene psychische Störungen, sondern auch mögliche Vorboten, wie z.B. Einsamkeit, verursachen Leid und können mit ungesundem Lebensstil und körperlichen und seelischen Krankheiten einhergehen. Deshalb wurde der Zusammenhang zwischen Einsamkeit und Lebensstil, physischen und psychischen Krankheiten untersucht. Einsamkeit kam in allen Altersgruppen von Erwachsenen vor und ging mit ungesundem Lebensstil wie Rauchen oder ungenügender sportlicher Aktivität einher. Auch die körperliche und psychische Gesundheit war bei einsamen Menschen in der Schweiz beeinträchtigt.

Kapitel 4: Gesunder Lebensstil ist nicht nur direkt mit Gesundheit verbunden sondern auch mit gesundheitsbezogenem Verhalten, z.B. mit der Teilnahme an Screeningprogrammen. In diesem Kapitel wurde der Zusammenhang von gesundem Lebensstil mit der Teilnahme am Screening für Gebärmutterhalskrebs untersucht. Es wurde aufgezeigt, dass Adipositas, körperliche Inaktivität und „nicht auf Ernährung achten“ mit geringerer Teilnahme am Screening in der Schweiz verbunden war.

Kapitel 5: Genetische Prädispositionen haben auch einen Einfluss auf die Gesundheit, z.B. beeinflusst die Hautfarbe den Vitamin-D-Status. Die Sonne (UVB) stellt mit ihrer Produktion von Vitamin D die grösste Vitamin-D Quelle dar. Je nach Hautfarbe fällt die Produktion unterschiedlich aus. Deshalb wurden Daten von 204 Schwangeren im UniversitätsSpital Zürich erhoben, die Prävalenz von Vitamin-D-Mangel (< 20 ng/mL) bestimmt und der Zusammenhang zwischen Hautfarbe mit Vitamin-D-Mangel evaluiert. Knapp zwei Drittel der Frauen wiesen einen Vitamin-D-Mangel auf, und die Wahrscheinlichkeit eines Mangels war grösser in Frauen mit dunkler Hautfarbe.

In dieser Arbeit wurden bisher unbekannte Prävalenzen zu diversen gesundheitsbezogenen Faktoren für die Schweiz aufgezeigt und Zusammenhänge zwischen Lebensstil und Gesundheit untersucht. Die Resultate zeigen, dass Lebensstil und Gesundheit eng zusammenhängen; Lebensstiländerungen – z.B. das Einhalten der 5-am-Tag Empfehlung – kann einen positiven Effekt auf die Gesundheit haben. Auch bzgl. einem unerwünschten emotionalen Zustand wie Einsamkeit kann es sinnvoll sein, bereits eine Änderung anzustreben, bevor möglicherweise eine manifeste psychische oder körperliche Erkrankung daraus entsteht. Insbesondere in Anbetracht der Zunahme des durchschnittlichen Lebensalters und der damit verbundenen Zunahme von NCDs ist es sinnvoll, einen gesunden Lebensstil zugunsten von physischer und psychischer Gesundheit anzustreben. Jedoch müssen die Resultate der vorliegenden Arbeit aufgrund des Querschnittsdesigns in zukünftigen populations-basierten Kohorten im Längsschnitt bestätigt werden.

INTRODUCTION

Introduction

This thesis evaluates several associations of health-related factors and lifestyle with health in Switzerland. The introduction part first gives an overview of the public health relevance and epidemiology of lifestyle and health in general, and second, illustrates the situation in Switzerland.

The public health relevance and epidemiology of lifestyle and health

Global perspective on health

According to the constitution of the World Health Organization (WHO) from 1946 health is not only understood as the absence of illness but as the state of complete physical, mental and social well-being (1). Thus, health of an individual not only depends on its genetic and biological predispositions but also on the social, cultural and ecological environment, on lifestyle, on behavior and on the available services of the healthcare system. Impaired health leads to morbidity or even premature mortality. Therefore, it is a major public health concern to assess the prevalence of different aspects of health and disease, and to evaluate how the risk of morbidity and premature mortality can be diminished. A great effort was made by the global burden of diseases, injuries, and risk factors study (GBD) to measure prevalences and trends worldwide from 1990 to the present in over 180 countries (2). As shown in Figure 1, three main groups of diseases are differentiated: non-communicable diseases; communicable diseases, maternal, neonatal, and nutritional diseases; and injuries. A common measure to describe the overall-burden of diseases, i.e., to quantify the burden of diseases, injuries and risk factors, and to make them comparable worldwide, are disability-adjusted life years (DALY). They are defined as the number of years of potential life lost due to early death (years life lost [YLL]) and the years of productive life lost due to disability (i.e. years lived with disability [YLD]).

Figure 1 shows that NCDs account for most DALYs (NCDs are represented by blue color, communicable, maternal, neonatal, and nutritional diseases by red color, and injuries by green color). Additionally, a strong annual increase in DALYs since 1990 was observed for many NCDs. NCDs include mental health, of which depression accounts for the largest amount of DALYs compared to the other mental diseases. Nevertheless, communicable,

INTRODUCTION

maternal, neonatal, and nutritional diseases also still have a great impact on DALYs worldwide.

In this thesis, four chapters will focus on lifestyle and NCDs including mental diseases, and one additional chapter on nutritional deficiency.

Figure 1: Worldwide disability-adjusted life years (DALY)

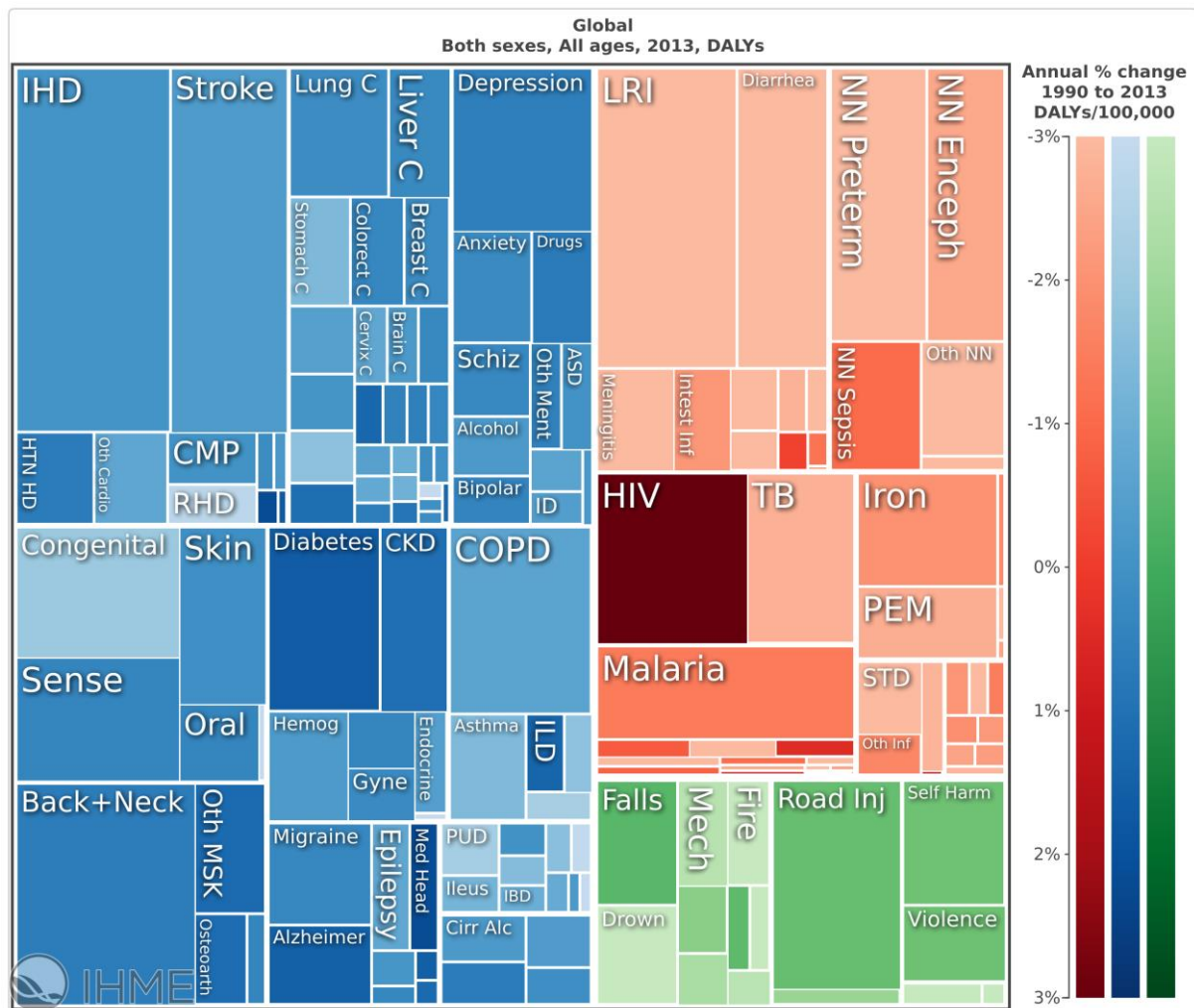


Figure legend: Blue color stands for noncommunicable diseases, red color for communicable, maternal, neonatal, and nutritional diseases, and green color for injuries (2)

INTRODUCTION

Noncommunicable disease and mental diseases

NCDs are non-transmittable diseases and most of them are chronic. Thus, they are sometimes referred to as chronic diseases. Chronic conditions, which are largely dependent on lifestyle, have become the major cause of death during the last century. Data from the Global Burden of Disease study from 2013 showed that worldwide the number of deaths from NCD increased by 42% between 1990 and 2013, due to the aging and growth of the population during this time period. But it should be noted that age-standardized mortality rates have decreased since 1990 with a median percentage change of minus 19% globally. Changes were more frequent in high- and middle- than in low- income countries. Concerning morbidity, YLD total numbers increased by 54% from 1990 to 2013 worldwide. However, age-standardized YLD rates from all NCDs increased by only 1.4% from 1990 to 2013 (3).

As stated by the WHO “Noncommunicable diseases, also known as chronic diseases, [...] are of long duration and generally slow progression. The four main types of noncommunicable diseases are cardiovascular diseases (e.g. heart attacks and stroke), cancers, chronic respiratory diseases (such as chronic obstructive pulmonary disease and asthma) and diabetes” (4). The Global status report on NCDs states that 42% of the premature death due to NCDs are considered to be preventable (5). As a consequence, the WHO global status report of noncommunicable diseases from 2014 defined 9 global targets on prevention and control (5). The first of these global targets aimed at a relative reduction in the overall mortality from the four main types of diseases, and the other targets are dedicated to lifestyle changes, such as relative reduction in harmful use of alcohol and salt intake, relative reduction in prevalence of insufficient physical activity or in current tobacco use.

Neuropsychiatric disorders accounted for more than a quarter of the non-fatal disease burden in the first global burden of disease study in 1990. As a consequence, mental health has gained increasingly more global attention. Neuropsychiatric disorders include neurological, mental, and substance use disorders as well as dementia. It has been shown that mental and substance use disorders were the leading causes of YLD worldwide (6). Accordingly, the WHO stated that worldwide 25 % of individuals develop one or more mental or behavioral disorders during their lifetime (7). A summary including systematic reviews, re-analyses of existing data sets and national survey results concluded that the 12-months prevalence for suffering from mental disorders was 38% in the European population. Anxiety disorders (14.0%), insomnia (7.0%) and major depression (6.9%) are the most

INTRODUCTION

frequent disorders in Europe. Depending on age and sex, percentages vary. For example, in women aged 15 to 44 years depression is the leading cause of mental disorders (8).

The WHO's comprehensive mental health action plan 2013-2020 was developed based on an increased commitment by governments for the necessity to consider mental diseases as important as other diseases. The action plan aims to put forward the prevention of mental disorders by providing an ambitious vision of a world in which mental health is valued and promoted. Key objectives were defined and included, such as strengthening of evidence and research for mental health (9).

Nutritional deficiencies (malnutrition)

Nutritional deficiencies have a variety of underlying causes. Insufficient intake of certain foods, nutrients or the inability of the body to absorb nutrients, such as vitamins and minerals, or increased losses of these nutrients might result in nutritional deficiencies, also known as malnutrition. Malnutrition has a major impact on morbidity and mortality, especially in less developed countries. Worldwide, protein-energy malnutrition (see PEM in Fig.1) accounts for 0.85% of total deaths. Marginal nutritional deficiencies are also observed in western countries and according to the WHO, some of these nutritional deficiencies are still causes of mortality in developed countries (10, 11).

Vitamin D deficiency - as an example of malnutrition –is still relevant also in developed countries. During the last century, vitamin D fortification programs have largely eradicated health risks of vitamin D deficiency such as rickets and osteomalacia from western populations. However, severe vitamin D deficiency (<20 ng/ml) is reemerging and suboptimal vitamin D blood levels are widespread in industrialized nations, especially in women with darker skin color (12-18). Furthermore, suboptimal vitamin D level is thought to be associated with a range of diseases such as cardiovascular disease, diabetes (19) and several types of cancer (20). It is thought that some chronic diseases, such as cancer or metabolic disorders, have their origins in early life and even in utero. Barker et al. (21) suggested that fetuses react and adapt to their nutrient supply during prenatal growth with consequences for the risk of chronic diseases later in life.

INTRODUCTION

Lifestyle

The roots of the term lifestyle used by poets, naturalists, and philosophers were traced back to the early sixteenth century (22). But the use of lifestyle as a construct of social sciences was probably first defined by the Austrian psychologist Alfred Adler (1879-1937), who was the founder of the individual psychology. He considered an individual as a “whole”, including the patient's environment, which had an influence on the development of an individual's personality trait. With respect to this background, lifestyle was defined as a style of personality, as a result of the individual's evaluation of the world (22). In the following, the construct of lifestyle became more prominent in different scientific fields such as history, philosophy, psychology and medicine. Nevertheless, it is still understood and defined heterogeneously among these fields, but all theories recognized that lifestyle might impact health in general as well as morbidity and even mortality. However, the association between lifestyle and health is very complex and reciprocal: health depends on lifestyle but health status can also impede or support a healthy lifestyle. There is convincing evidence that age, gender and socioeconomic status have a strong impact on lifestyle, but these are rather non-modifiable factors. Thus, lifestyle is not only an individual's choice but depends on historical, cultural as well as economic and social factors (23). In contrast, the term lifestyle used in medical sciences – which is the way how lifestyle is defined in this thesis - mostly refers to modifiable lifestyles, such as physical activity, dietary habits, smoking, and alcohol consumption, but also the use of preventive measures (e.g. cancer screening participation) and prevention of nutritional deficiencies (e.g. vitamin D deficiency).

In 1986, the WHO defined lifestyle as behavioral choice dependent on circumstances the individuals live with. Nowadays, the WHO gives recommendations about healthy lifestyle, such as eating lots of fruits and vegetables, reducing fat, sugar and salt intake, non-smoking and sufficient physical activity (5).

Lifestyle and health in Switzerland

Life expectancy in Switzerland is the highest in Europe with an average life expectancy at birth of 82.8 years (80.7 years for men and 84.9 years for women, respectively) (24).

Thus, morbidity and chronic conditions are a major concern in the ageing society of Switzerland. According to the Global Burden of Disease study 2013 in Switzerland NCDs account for more than 85% of the burden of disease. Cardiovascular diseases (CVD) and

INTRODUCTION

cancer are the two major causes of mortality, although the age-standardized mortality rates decreased in Switzerland in the last years (24).

In 2012, 32% of the Swiss population was affected by a chronic disease (25). Chronic diseases are more frequent in older age and half of the population above 50 years reported at least one medically diagnosed chronic disease (25). Men had a higher risk than women for NCDs in 2012 due to more risk behavior concerning diet, alcohol consumption, smoking, high body mass index (BMI), diabetes, hypertension and high cholesterol blood levels (26). Further known risk factors are demographic factors, such as low salary, low education, and migration status (25). It is estimated that obesity contributes to excess in death of about 7% and smoking of about 12% in Switzerland (27, 28).

Switzerland appears to be slightly “healthier” with respect to lifestyle than the European average, e.g. for smoking and obesity (24). But still nearly one third of men and 24% of women are smoking. Almost one third of the population is overweight ($\text{BMI} \geq 25$ and $< 30 \text{ kg/m}^2$) and 10% are obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). Chronic risky alcohol consumption (women $\geq 20 \text{ g}$ ethanol and men $\geq 40 \text{ g}$ ethanol) is reported by 5% of the population in Switzerland, and insufficient physical activity (defined as <150 min per week moderate physical activity and/or one sweating episode per week vs. more) by 27% of the population (29).

Data collection in Switzerland

Switzerland is a small country with about 8 million inhabitants, which has a highly decentralized and complex health system. Data about lifestyle and health for individuals living in Switzerland is not collected on a national level with some exceptions, such as causes of death and stillbirth, which are collected by the Swiss Federal Statistical Office (FSO) (30), and the national incidence cancer registration (NICER) (31), which does not cover all cantons. Furthermore, a variety of registries for some NCDs were established. To mention some, there is the National Registry of Acute Myocardial Infarction in Switzerland (AMIS Plus) (32) including 50,000 patients, and the Swiss transplant cohort study (STCS) (33) that aims to have one unique data basis for all solid organ transplant recipients.

There is no longitudinal nationwide epidemiological cohort study in Switzerland investigating the interplay between lifestyle and health. However, some efforts in Switzerland were made to implement epidemiological longitudinal cohort studies, such as the Swiss Study on Air Pollution and Lung Disease in Adults (SAPALDIA) (34). This study

INTRODUCTION

investigates the associations of genetic and modifiable environmental factors in a broad range of chronic diseases including respiratory, allergic, cardiovascular disease since 1991 in about 10,000 adults from eight different Swiss areas having distinct degrees of air pollution exposure and diverse climate. Another ongoing cohort study with over 6,000 participants is the CoLaus/PsyColaus study from Lausanne that started in 2003, with the aim to obtain information on the epidemiology and genetic determinants of cardiovascular risk factors and diseases as well as mental health in the adult population of Lausanne (35, 36). In 2009, the Zurich Program for Sustainable Development of Mental Health Services (ZInEP) was established that focuses on the interface between research and care for mental health. The program targets 10,000 patients with primarily serious illnesses and the need for complex care (37).

Besides the above mentioned cohort studies and other regional cohort studies with smaller numbers of participants, Switzerland has a long-term, census-based, multipurpose cohort and research platform - the Swiss National Cohort (SNC), in which all residents of Switzerland participate. It is based on the linkage of individual data from the 1990 census with the 2000 census and mortality data. However, only a few variables are collected, most of them are demographics such as age, sex, and household size. The second largest study conducted in Switzerland is the representative population-based Swiss Health Survey (SHS) that is carried out every 5 years by the FSO (38). This survey aims to gather information on health status, health behavior and the use of health services and as a consequence, to plan and evaluate health policy strategies and measures in prevention and health promotion. The SHS is based on registries of inhabitants and on the availability of landline telephone; data were collected by telephone interview and an additional written questionnaire upon approval from the participants. The participation rate ranged from 71% in 1992 to 54% in 2012. The SHS 2012 is the database used for chapter 1 to 4 in this thesis.

Aims of the thesis

For this thesis, we used data from the population-based SHS – with the exception of the last chapter on vitamin D – to provide unknown prevalence rates of health related factors and diseases and to evaluate possible associations between health and lifestyle for the population living in Switzerland. The multifaceted and complex associations between

INTRODUCTION

lifestyle, physical and mental health are emphasized in this thesis by providing the following 5 chapters.

Chapter 1: Assessing whether not adhering to the widely known 5-a-day campaign for fruit and vegetable consumption is associated with psychological distress

Diet is an important modifiable factor that can affect health in various ways. The aim was to assess the associations of adhering to the 5-a-day recommendations for fruit and vegetables consumption with psychological distress.

There is growing evidence that diet has a beneficial effect on the occurrence and recurrence of mental diseases, such as depression (39, 40). Previous research focused on single nutrients, before, focusing single dietary components and dietary patterns, such as the Mediterranean diet (41, 42). These days in many countries including Switzerland dietary recommendations exist and are broadly promoted. These recommendations were originally developed to enhance an individual's physical health (43), but mental health was generally not a topic of interest. One of the most famous recommendations is the so-called 5-a-day recommendation for fruit and vegetables, which is promoted since 2001 in Switzerland. The definition of this recommendation was derived from the WHO Global Strategy on Diet, Physical Activity and Health and vary slightly between different countries (44). In Switzerland, dietary recommendations are based on the Swiss Nutrition Society (43). Compliance with dietary recommendations among adults in Switzerland is low (45). To our knowledge the associations between 5-a-day recommendations and mental health have not been evaluated yet, neither worldwide, nor in Switzerland.

We analyzed data from the 2012 SHS and included 20,220 individuals aged 15 years and above. Information about fruit and vegetable consumption was based on consumption frequency. The recommended portions per day were defined as 5-a-day (at least 2 for fruit and 3 for vegetables). The outcome was perceived psychological distress over the previous 4 weeks measured by the 5-item mental health index (MHI-5).

Our results provide information on the associations between adhering to the 5-a-day recommendation and psychological distress. They support the public health relevance of existing recommendations with the aim to support or enhance healthy lifestyle (46).

Chapter 2: Examining the associations of body weight dissatisfaction with depression in individuals of different sex, age, and with different body mass index

A variety of intrapersonal factors influence an individual's satisfaction with one's life or single aspects of life, such as feelings, attitudes, perceptions, and behaviors. Thus, they can affect health, even mental health. We aimed to examine if body weight dissatisfaction (BWD) is a risk factor for depression.

Body image dissatisfaction is very common in adolescents and adults. Up to one third of German men and nearly half of German women are affected (47, 48). Body image has been shown to be associated with eating disorders, but also in the context of mental health and depression, as an important public health problem (49, 50). The associations have primarily been observed in adolescents (51-56).

We examined the association of dissatisfaction with body weight, as a component of body image with depression overall, in men and women as well as in young, middle-aged and old individuals independent of body weight. We analyzed data of the Swiss Health Survey 2012 including more than 16,000 adults. Participants were asked about their body weight dissatisfaction. Patient Health Questionnaire was used to assess depression.

Our results are of importance for public health strategies, but need to be confirmed in prospective studies, before body weight dissatisfaction could be used as a factor in the prevention of depression.

Chapter 3: Considering loneliness - a common emotional distress experience - and its associations with lifestyle, physical and mental health

Not only manifest psychiatric disorders but also more general concepts or precursors, such as loneliness, are common in the population and may be associated with unhealthy lifestyle and physical and mental illness. Thus, we evaluated whether loneliness is associated with health outcomes.

Loneliness is caused by the felt sense of social isolation and unsatisfied need for affection in current relationships (57, 58). In this chapter, the associations of loneliness with lifestyle and physical and mental health were examined. Loneliness can be a long-lasting perception with negative behavioral and health outcomes (59, 60). Although loneliness is a common emotional experience (61), little is known about the prevalence of loneliness in different age

INTRODUCTION

groups, and about age and sex as potential effect modifiers of the association between loneliness and lifestyle or health-related factors. Furthermore, most studies looking at the associations of loneliness with health stem from North American cohorts, thus, it is worthwhile to investigate these associations also for Switzerland with a population-based data approach.

The aim of the study was to examine the prevalence of loneliness in individuals aged 15 years and above in Switzerland and to assess the associations of loneliness with behavioral, physical and mental health factors, taking sex and age into account. Data from 20,007 participants of the cross-sectional population-based SHS 2012 were used to assess the association of loneliness with lifestyle (e.g. smoking status, alcohol consumption) and health-related factors (diabetes, hypertension, cholesterol levels, prevalence of chronic diseases, self-perceived health, psychological distress, depression).

Our results provide new insights into the associations of loneliness with a variety of health related factors, most of them not investigated for Switzerland yet. From a public health perspective, it might be worthwhile to intervene, e.g. by providing population-based prevention programs, to raise the awareness of unpleasant emotional experiences as possible precursors of mental diseases, unhealthy lifestyle or physical illness.

Chapter 4: Examining lifestyle and health-related predictors of cervical cancer screening attendance

Healthy lifestyles are not only related to health directly but also to health behaviors, e.g. to participation in screenings. Thus, in this chapter, the association of healthy lifestyle with participation to cervical cancer screening was examined.

Cervical cancer, for example, is the second most common cancer in women worldwide, although incidence and mortality have decreased markedly (62, 63) in the last 30 years. Little is known about predictors of cervical cancer screening attendance, except for the influence of demographic factors such as age, educational level and marital status (64-66). In Switzerland, which is characterized by a broad, opportunistic screening system, cervical cancer screening has been promoted since the late 1960s. For cervical cancer screening there is no organized program in Switzerland and the cervical cancer screening time interval depends on the doctor's personal judgment. The Swiss Federal law of health insurance

recommends one Pap smear every three years after two annual negative results from the age of 18 until 69 years (67).

We examined the association of lifestyle and health-related factors with attendance to cervical cancer screening. Lifestyle factors included body mass index, smoking status, alcohol consumption, physical activity and attention to diet. Health-related factors of interest were diabetes, hypertension, high cholesterol levels, chronic diseases, self-perceived health, and psychological distress. We analyzed the data of 18-69 years old women (n=7,319) from the SHS 2012.

Our results support the importance of improving the cervical cancer screening practices of low user groups in Switzerland (68).

Chapter 5: Assessing the prevalence of vitamin D deficiency and its association with skin color of women in early pregnancy living in the area of Zurich

Genetic predispositions also have an impact on health, such as skin color might affect vitamin D concentrations in the body.

Vitamin D deficiency in pregnancy has been shown to be associated with a variety of clinical consequences that range from negative influence on glucose tolerance, association with preeclampsia to improvement of birth weight by vitamin D supplementation in certain ethnic groups (69, 70). Furthermore, in pregnancy, increased calcium and adequate vitamin D levels are required and, thus, pregnant women may be at higher risk of vitamin D deficiency. Several studies showed that personal characteristics affect vitamin D synthesis, such as the skin color. The circulating vitamin D concentrations differ by skin color, i.e. individuals with darker skin produce less vitamin D with the same amount of sunlight exposure than individuals with lighter skin color (71, 72).

The aim of our study was to evaluate vitamin D levels in pregnant women and to determine the prevalence of vitamin D deficiency (< 20 ng/mL). Furthermore, we aimed at addressing the question whether the prevalence of vitamin D deficiency differs between women with light or dark skin color, i.e., between specific subgroups of the population living in Switzerland.

Pregnant women (n=204), who attended the Clinic of Obstetrics at the University Hospital Zurich (Switzerland) for their first pregnancy visit (week 6 to 10 of pregnancy) were included

INTRODUCTION

in our study. Validated Fitzpatrick scale and objective melanin index was used to determine skin color.

Our results contribute to the lack of knowledge on the prevalence of vitamin D deficiency in pregnant women living in Switzerland. Furthermore, our result may contribute to support more intense counseling of pregnant women and of women planning to become pregnant to improve their vitamin D status, for example by using vitamin D supplements during pregnancy, in particular for women with darker skin color.

Contributions of the thesis defendant to the work presented

Chapter 1: I planned and performed the analysis and drafted the manuscript.

Chapter 2: I planned and performed the analysis and drafted the manuscript together with Monika Eichholzer.

Chapter 3: I planned and performed the analysis and drafted the manuscript.

Chapter 4: I planned and performed the analysis and drafted the manuscript.

Chapter 5: I was part of the team planning and conducting the study. I was responsible for the first draft of the study protocol as well as data entry and data preparation. For the presented analyses in this chapter I planned and performed the analysis and drafted the manuscript.

All my work has been supervised by Sabine Rohrmann.

Introduction

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INTRODUCTION

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CHAPTER 1

Associations between fruit and vegetable consumption and psychological distress: results from a population-based study

Aline Richard^{1, 3}, Sabine Rohrmann¹, Caroline L. Vandeleur², Meichun Mohler-Kuo¹, Monika Eichholzer¹

¹ Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Hirschengraben 84, CH-8001, Zurich, Switzerland

² Centre for Research in Psychiatric Epidemiology and Psychopathology, Department of Psychiatry, University Hospital of Lausanne, Site de Cery, 1008, Prilly, Switzerland

³ Corresponding author

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Abstract

Background: Several studies observed associations of various aspects of diet with mental health, but little is known about the relationship between following the 5-a-day recommendation for fruit and vegetables consumption and mental health. Thus, we examined the associations of the Swiss daily recommended fruit and vegetable intake with psychological distress.

Methods: Data from 20,220 individuals aged 15+ years from the 2012 Swiss Health Survey were analyzed. The recommended portions of fruit and vegetables per day were defined as 5-a-day (at least 2 portions of fruit and 3 of vegetables). The outcome was perceived psychological distress over the previous 4 weeks (measured by the 5-item mental health index [MHI-5]). High distress (MHI-5 score ≤ 52), moderate distress (MHI-5 > 52 and ≤ 72) and low distress (MHI-5 > 72 and ≤ 100) were differentiated and multinomial logistic regression analyses adjusted for known confounding factors were performed.

Results: The 5-a-day recommendation was met by 11.6% of the participants with low distress, 9.3% of those with moderate distress, and 6.2% of those with high distress. Consumers fulfilling the 5-a-day recommendation had lower odds of being highly or moderately distressed than individuals consuming less fruit and vegetables (moderate vs. low distress: OR=0.82, 95% confidence interval [CI] 0.69-0.97; high vs. low distress: OR=0.55, 95% CI 0.41-0.75).

Conclusions: Daily intake of 5 servings of fruit and vegetable was associated with lower psychological distress. Longitudinal studies are needed to further determine the causal nature of this relationship.

Keywords: psychological distress; mental health; 5-a-day recommendation; fruit; vegetables

Introduction

Mental diseases are a leading cause of the global burden of disease and highly contribute to life-years lost (Ferrari et al., 2013, Whiteford et al., 2013). According to the World Health Organization (WHO), worldwide 25% of individuals develop one or more mental or behavioral disorders during their lifetime (Kessler et al., 2009).

Acute and chronic stress are considered to be potential risk factors for mental disorders, including depression and anxiety, depending on the individual's stress sensitivity (Bale, 2006, Colman et al., 2014). There are several definitions of stress and/or psychological distress, which share the point of view that it is expressed by emotional suffering (Horwitz, 2007).

There is growing evidence that modifiable lifestyle factors, particularly diet, have a beneficial effect on the occurrence and recurrence of mental diseases, such as depression (Ruusunen et al., 2014, Sanhueza et al., 2013). Nevertheless, associations between diet and mental health are evaluated by a variety of different aspects, such as focusing on single dietary components, dietary patterns or on single nutrients (Akbaraly et al., 2009, Quirk et al., 2013, Rahe et al., 2014, Rienks et al., 2013, Giles et al., 2013).

In fruit and vegetables, there are a large number of bioactive compounds that could be responsible for an effect on mental health (Miller et al., 2000). Nevertheless, only a few studies explicitly examined the association of fruit and vegetable intake with mental health, but these studies observed inverse associations (Payne et al., 2012, McMartin et al., 2013).

The 5-a-day recommendation is one of the best-known dietary campaigns to date, which takes fruit and vegetable intake into account and was implemented in the 1990s by the National Cancer Institute in the U.S. In the following years, many western countries engaged in similar campaigns (e.g. Germany, Great Britain, France). In Switzerland, the 5-a-day campaign started in 2001 and is defined by consuming at least 3 portions of vegetables and 2 portions of fruit daily. Other countries have slightly different definitions of 5-a-day (e.g. 5 daily portions without defining whether fruit or vegetables in France). Definitions rely on the WHO Global Strategy on Diet, Physical Activity and Health that recommends "a minimum of 400g of fruit and vegetables per day (excluding potatoes and other starchy tubers)" (WHO, Fruit and Vegetable Promotion Initiative - report of the meeting, Geneva, 25-27 August 2003). To our knowledge, associations between 5-a-day recommendations and mental health have not been evaluated yet. Thus, given the paucity of research on the topic, it is

worthwhile to evaluate whether the 5-a-day recommendation has a positive effect on mental health. Our aim was to examine the association between the adherence to the 5-a-day recommendation and psychological distress in the Swiss population.

Methods

Study population and data

Data were obtained from the Swiss Health Survey (SHS) conducted in 2012/2013 by the Swiss Federal Bureau of Statistics (SFSO). All data used for this study were collected by telephone interview. The data collection and data storage for the Swiss Health Survey does not require formal approval by an ethical committee. This data collection is specifically permitted under Swiss law (SR 431.012.1 and SR 431.112.1). Individuals invited to participate received a brief description of the study and could decline to participate or withdraw at any time. Participants' responses were treated confidentially and aggregated anonymous responses were utilized for analyses presented herein.

The SHS is a cross-sectional, population-based nationwide survey on health status, several lifestyle and demographic factors, and healthcare use and has been carried out every five years since 1992. Using a stratified random sampling technique based on registries of inhabitants, individuals aged 15 years or older and living in a private household were recruited. A total number of 21,597 individuals participated, derived from an initial sample of 41,008 individuals (participation rate 54%). A computer-assisted telephone interview (CATI) was performed and in a further step, a written questionnaire was provided (paper or online) upon approval from the participants (n=18,357) (Swiss Federal Statistical Office). This multistage probability sample can be considered as representative of the Swiss population.

Information on the mental health index (MHI-5) was available for 20,652 individuals. Individuals with missing information on fruit and vegetable consumption were excluded from analyses (n=90). In a further step, we excluded individuals with missing information on covariates, such as age or education level etc. (n=342), resulting in a final sample of 20,220 participants.

Outcome measure

The outcome of interest was psychological distress measured by the 5-item mental health index [MHI-5] (Berwick et al., 1991). The five-item Mental Health Inventory (MHI-5) assessed the extent of perceived psychological distress during the previous 4 weeks. The MHI-5 is a valid tool to measure mental health in the general population and the five items assess how often over the past month individuals felt nervous, felt so down that nothing could cheer them up, felt calm and peaceful, felt down and blue, or felt happy (Trainor et al., 2013, Whang et al., 2009, Berwick et al., 1991). Answers were categorized according to a 5-point Likert scale ranging from „always” to „never”. The MHI-5 has shown good sensitivity and specificity for detecting DSM-IV Axis-I disorders in the general population (Rumpf et al., 2001).

The SFSO provided the linearly transformed scale for the MHI-5, which ranges from 0 to 100 (Swiss Federal Statistical Office, 2012). Studies have shown that scores below 53 indicate clinically relevant distress symptomatology (high distress), scores between 53 and 72 may indicate a higher probability of psychiatric symptoms but less than those for high distress (moderate distress), and scores above 72 are considered to represent good mental health status (low distress) (Kroenke et al., 2005, Hoeymans et al., 2004, Cuijpers et al., 2009). The use of these 3 categories has also been recommended by the SFSO (Swiss Federal Statistical Office, 2012).

Exposure measurements

Definitions of fruit and vegetable consumption were based upon food frequency questionnaires. For both fruit and vegetables, two questions were asked. The first question was related to frequency: „On how many days a week do you usually eat fruit or drink fruit juices?” or „On how many days a week do you usually eat vegetables or salad or drink vegetable juices (potatoes do not count)?”. Answers were coded as „less”, „rarely”, „1”, „2”, ... to „7” times a week. The second question was related to the number of portions consumed: “And how many portions of fruit or fruit juices do you consume on average per day? One portion would be as big as a handful (i.e. 1 apple, 1 pear). For juice it is about 2 dl.” and „And how many portions of vegetables, salad or vegetable juices do you consume daily on average? One portion would be as big as a handful (or about 1 tomato, 1 big carrot). For juice it is about 2 dl”. The second question was only asked if the first question was positive

for a frequency of at least “5 times a week” and answers were coded into „less than 1 portion”, and „1”, „2”, „3”, „4” and „5 portions or more”.

Based on the recommendations of the Swiss Nutrition Society (Schweizerische Gesellschaft für Ernährung SGE, 2013) we defined adherence to the recommended amount of fruit and vegetable consumption as at least two and three portions per day, respectively. Adhering to both the recommended fruit and vegetable consumption was defined as compliance with the 5-a-day recommendation.

Covariates

Sociodemographic variables and health behaviors that could influence the associations between fruit and vegetable consumption and psychological distress were examined as confounders and were included in the multivariable analyses. For body mass index (BMI), we differentiated between underweight, normal weight, overweight and obesity ($<18.5 \text{ kg/m}^2$, $18.5 - <25 \text{ kg/m}^2$, $25 - <30$, $\geq 30 \text{ kg/m}^2$, respectively) (WHO, 2013b). For individuals younger than 18 years, the tables of Cole et al. (2000) were used to define the four BMI categories. We additionally included age categories (15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 74+ years), gender, nationality (Swiss vs. foreigner), marital status (single, married, divorced/separated/widowed), educational level (low: compulsory education or less, middle: secondary education, high: tertiary education), smoking status (never, former, current), alcohol consumption ($\leq 20 \text{ g}$ ethanol per day for women, $\leq 40 \text{ g}$ for men vs. $> 20 \text{ g}$, $> 40 \text{ g}$, respectively) (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2010), physical activity ($\geq 150 \text{ min.}$ per week vs. less) (BASPO, 2013), and chronic diseases (hypertension or diabetes; yes vs. no). Other types of food consumption were further dichotomized into unfavorable vs. recommended according to the Swiss Nutrition Society depending on the information about consumption frequencies. We included meat (> 4 days per week vs. less), fish (never or less than one day per week vs. more) and dairy products (< 2 portions per day vs. more) (Schweizerische Gesellschaft für Ernährung SGE, 2013).

Statistical analyses

All statistical analyses were conducted using STATA software version 13.1 (College Station, Texas). Sociodemographic and health-related characteristics were computed using contingency tables stratified by level of psychological distress. We conducted maximum-

likelihood multinomial (polytomous) logistic regression analyses to determine associations between fruit and vegetable intake and levels of psychological distress (low vs. moderate and high, respectively). Results for multinomial regression analyses were computed in terms of relative risk ratios, but we use the term odds ratio (OR) to enhance comprehensibility. Four Models were conducted successively: 1) unadjusted, 2) adjusted for age and sex, 3) adjusted for demographic and health-related factors, and 4) adjusted for all the covariates in model 3 plus meat, fish and dairy product consumption. In order to draw valid conclusions regarding the Swiss population based on our sample, the SFSO made a comparison with the permanent 2012 Swiss population. All analyses were weighted by using the population-based weights of the telephone interviews provided by the Swiss Federal Office of Statistics. The weights are based on the 2012 Swiss population with respect to sex, age, geographic region and nationality (Swiss/non-Swiss); any differences caused by stratification or non-participation were mathematically corrected. Additionally, a sensitivity analysis was performed to compare non-included individuals who had information on their level of distress with those who were included in the present analysis. We also conducted an analysis that included interaction terms to assess the associations of sex and 5-a-day adherence with the psychological distress outcomes to determine whether the results differed between men and women.

Results

Table 1 shows socio-demographic and health-related characteristics stratified by levels of psychological distress into low (82%), moderate (13.4%), and high (4.6%). Among individuals with high distress levels, a higher percentage of individuals reported to be foreigners than individuals with moderate or low distress levels. A higher percentage of participants with high distress levels had a high level of education compared to individuals reporting low and moderate distress levels. Obesity tended to be reported more frequently by individuals with high distress levels than by individuals with low distress levels. A sensitivity analysis revealed similar distributions of sociodemographic characteristics stratified by psychological distress levels in individuals not included in this analysis (having missing information on fruit and vegetable consumption or confounders; n=432; data not shown).

As we did not observe any statistically significant effect modification by sex (all interaction terms > 0.05 ; data not shown), only the results of the overall sample are reported.

Figure 1 shows that the consumption of at least 3 portions of vegetables per day was reported by 18.3% and of at least 2 portions of fruit per day was reported by 35.7% of all individuals. The 5-a-day recommendation was fulfilled by 11.1% of all individuals, and when stratified by distress levels, was reported by a higher percentage of individuals with low distress compared to individuals with moderate or high distress levels.

Table 2 reveals that participants adhering to the recommended amount of vegetable consumption had a lower odds of reporting high distress levels compared to those who were non-adherent (odds ratio [OR] 0.64; 95% confidence interval [CI] 0.49-0.82, multivariable adjusted plus diet; Table 2). For moderate distress levels, these results were no longer statistically significant after multivariable adjustment.

We did not observe a statistically significant association between adherence to fruit consumption and the odds of high distress levels (OR 0.84; 95% CI 0.69-1.02), but participants who consumed the recommended amount of fruit were statistically significant less likely than those who were non-adherent to report moderate distress levels (OR 0.83; 95% CI 0.74-0.9, multivariable adjustment plus diet; Table 2).

Adhering to the 5-a-day recommendation was statistically significantly associated with high and moderate distress levels compared to non-adherence throughout all the models. In the multivariable adjusted model plus diet, e.g., adhering to the 5-a-day recommendation was statistically significantly associated with lower odds of high distress (OR 0.55; 95% CI 0.41-0.75) and moderate distress levels (OR 0.82; 95% CI 0.69-0.97), respectively.

Discussion

In this large population-based Swiss survey we observed significant inverse associations between fruit and vegetable consumption and distress levels. Individuals keeping to the 5-a-day recommendation had a lower likelihood to report moderate or high distress levels than individuals not adhering to the 5-a-day recommendation. To our knowledge, this is the first time associations of this type are reported in Switzerland. Our results are in line with the few existing Western country studies on the effect of fruit and vegetable intake on mental

health. In a cross-sectional random sample of nearly 1000 primary care patients in the US, Rohrer et al. (Rohrer and Stroebel, 2009) observed that a higher self-reported quantity of fruit and vegetables per day was associated with lower mental distress. McMartin et al. (McMartin et al., 2013) also observed an association between fruit and vegetable consumption and mental health using five waves of a national cross-sectional Canadian survey. A recent cohort study on women's health from Australia found an inverse effect of fruit and vegetable consumption on incident depression after a 6-year follow-up (Mihirshahi et al., 2014). Another 12-year follow-up study in a cohort of generally healthy Australian men and women observed that adherence to a Mediterranean-style diet was associated with less psychological distress at follow-up (Hodge et al., 2013).

A recent review of observational studies including cohort, case-control and cross-sectional studies came to the conclusion that "healthy" and Mediterranean dietary patterns seem to lower the likelihood of depression (Rahe et al., 2014, Kuczmarski et al., 2010). An important part of a Mediterranean diet is a high intake of fruit and vegetables (Ferrari and Rapezzi, 2011). In a number of studies, diet quality was evaluated in relation to depression (Gougeon et al., 2015, Jacka et al., 2014, Le Port et al., 2012). However, dietary patterns were assessed quite heterogeneously. Additionally, in studies primarily looking at single dietary components, such as fruit and vegetables, analyses were often not controlled for other dietary or lifestyle factors (Payne et al., 2012, McMartin et al., 2013, Jacka et al., 2010).

In our study, we performed two sets of multivariable analyses, i.e. one including age, sex, education, nationality, smoking status, physical activity and chronic diseases and an additional one further including additional dietary factors, i.e., consumption of fish, meat, and dairy products, as potential confounders. The results remained similar, thus, strengthening the evidence that healthy fruit and vegetable consumption might be responsible for the observed inverse association with mental distress.

Fruit and vegetables are rich in antioxidants such as vitamin C, vitamin E, carotenoids, phenolic compounds etc. (Miller et al., 2000). Antioxidants have two main effects. First, they reduce oxidative stress (Rink et al., 2013). Oxidative stress, in turn, has consistently been shown to be increased in chronic stress and depression (Manosso et al., 2013). Second, antioxidants in diet can decrease inflammation such as cytokine production (Giugliano et al., 2006, Rink et al., 2013). There is some evidence that cytokine production is elevated in stress and depression, but the higher concentrations could also be the consequence of additional

diseases or the consumption of drugs (Milaneschi et al., 2012, Glaus et al., 2014). Nevertheless, studies examining the association of antioxidants with depression are still rare but seem to support an inverse association. For example, the InCHIANTI cohort study found that low plasma concentrations of carotenoids were significantly associated with incident depression in older individuals over a 6-year follow-up (Milaneschi et al., 2012).

Folate is a further substance in fruit and vegetables that has been shown to be linked to depression. A meta-analysis of observational studies showed significant inverse associations of folate status with depression (Gilbody et al., 2007). The included studies were mostly cross-sectional, but the result was also supported by one cohort study (Gilbody et al., 2007). The latter study hypothesized that folate increases methylation processes and the regulation of neurotransmitters, such as serotonin which, in turn, is associated with a lower risk of depression.

Strengths and Limitations

Our analyses were based on the MHI-5, whereas research on diet and depression is more common than on diet and mental distress in general. However, the MHI-5, which assesses distress over the previous 4 weeks, was compared to clinical interviews as the gold standard and has been shown to be a valid tool to detect depression in the general population as well as in psychiatric surveys (Rumpf et al., 2001, Berwick et al., 1991, Cuijpers et al., 2009). Furthermore, our results may have practical implications not only for individuals with high psychological distress, who, according to the MHI-5 would receive a diagnosis of mental disorders, but also for individuals with moderate distress, who are considered vulnerable to the development of mental disorders, especially depression and anxiety (Bale, 2006).

A further strength of our study is the multivariable adjustment for potential confounders, and in particular for other dietary factors. In most fruit and vegetables, omega-3 fatty acid concentration is negligible, but there is a large amount of omega-3 fatty acids in some types of fish, which were mostly associated with depression in cross-sectional and prospective epidemiological studies as well as in randomized controlled trials (Sanhueza et al., 2013, Giles et al., 2013). We partly accounted for this by adjusting our analysis for fish consumption and our results remained unchanged. Nevertheless, residual confounding, and confounding due to other dietary factors such as energy intake, which were not assessed in the SHS, cannot be excluded. Additionally, the questions about diet were not validated. A

further limitation is that the direction of the association cannot be derived, due to our cross-sectional design. It might be possible that the presence of mental distress could result in dietary changes (Mikolajczyk et al., 2009). This is for example supported by the possibility of “loss of appetite” in depressive episodes as defined in the international statistical classification of diseases and related health problems (ICD-10) (World Health Organisation, 1992) which may affect eating patterns. However, the results of two prospective studies, have strengthened the evidence that healthy diet (Lai et al., 2014) and fruit consumption in particular (Mihirshahi et al., 2014) have an impact on subsequent mental health.

Conclusions

Keeping to the 5-a-day recommendation was associated with lower psychological distress. Thus, strengthening efforts to comply with this dietary recommendation would be an effective and cost-effective means to lowering psychological distress. Nevertheless, these findings warrant confirmation in prospective studies, specifically to establish the temporal sequence of this association.

Ethical standards: Legal basis: Ordinance of the Conduct of Federal Statistical Surveys of June 30, 1993

Conflicts of interest: The authors declare that they have no conflict of interest.

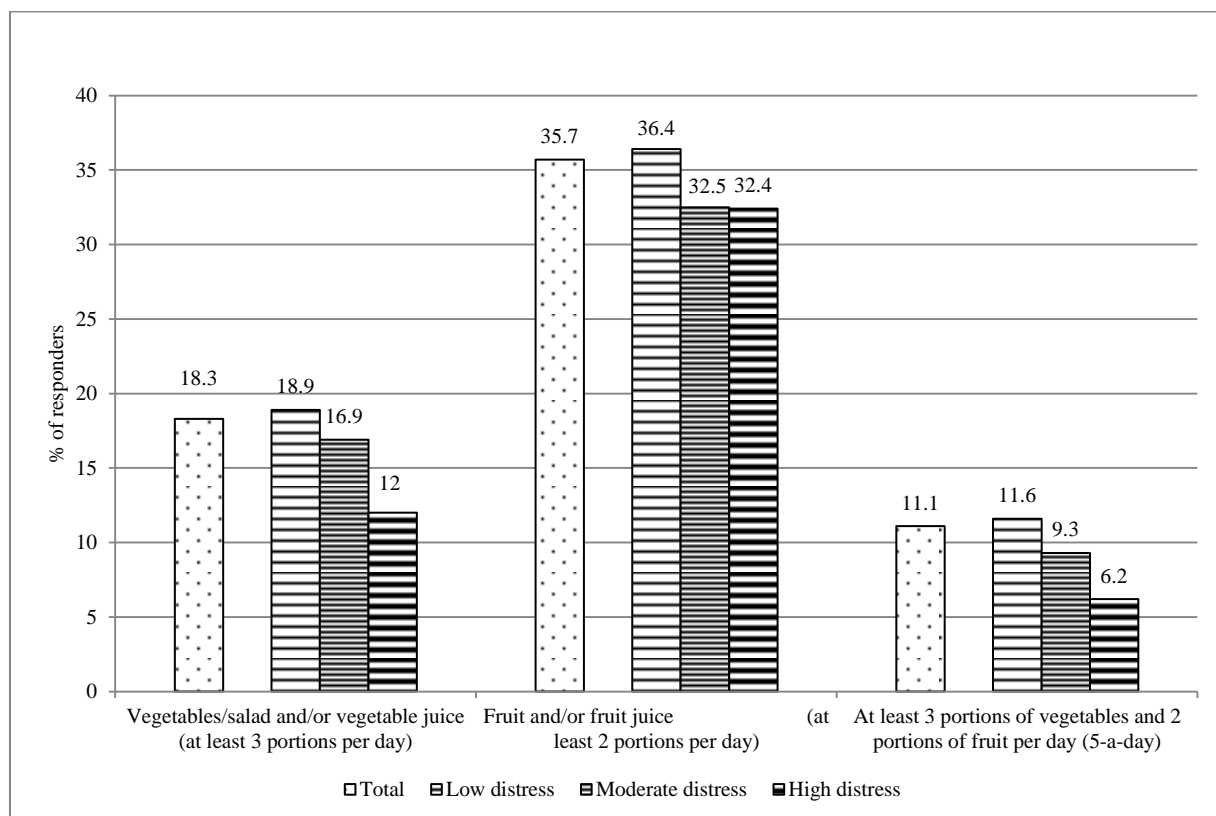
Authors Contribution: AR and ME designed the study. AR wrote the manuscript and performed the statistical analyses. All authors (AR, SR, CLV, MMK and ME) contributed to the interpretation of the data and edited the manuscript. ME supervised the study. All authors contributed to and have approved the final manuscript.

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Chapter 1

Tables and Figures

Fig. 1 Consumption of fruit and vegetables overall and stratified by psychological distress level of the Swiss Health Survey 2012



CHAPTER 1

Tab. 1: Characteristics¹ of the participants stratified by psychological distress levels² from the Swiss Health Survey 2012

Distress level		low	moderate	high
n, unweighted		16,552	2,721	947
		47.0	46.8	
Age (years), mean (SD)		(0.18)	(0.50)	46.6 (0.67)
		%	%	%
Total		82.0	13.4	4.6
Age (years)	15-24	13.8	13.2	8.9
	25-34	15.6	17.1	16.4
	35-44	16.7	17.1	20.1
	45-54	19.2	18.4	24.4
	55-64	13.8	14.7	15.2
	65-74	11.9	9.1	9.1
	75+	9.0	10.3	5.9
Nationality	Swiss	80.3	73.4	68.2
	Foreigner	19.7	26.6	31.8
Marital status	Single	32.6	32.3	29.6
	Married	51.6	48.2	46.3
	Divorced/separated/widowed	15.8	19.5	24.1
Educational level	Low	14.7	21.0	27.7
	Middle	54.2	54.8	54.8
	High	31.2	24.2	17.4
BMI kg/m ²	< 18.5	3.4	4.0	5.3
	≥ 18.5 - < 25.0	56.3	54.9	50.4
	≥ 25.0 - < 30.0	30.7	30.6	29.8
	≥ 30	9.6	10.5	14.4
Smoking history	Never	51.2	45.4	39.6
	Former smoker	22.0	21.5	17.1
	Current smoker	26.8	33.1	43.4
Moderate physical activity	< 150 min. per week	24.5	36.0	45.1
	≥ 150 min. per week	75.5	64.0	54.9
	Hazardous chronic			
Alcohol consumption ³	consumption	4.7	6.0	4.2
	Lower consumption or none	95.3	94.0	95.8
Chronic diseases ⁴	No	73.1	69.2	67.3
	Yes	26.9	30.8	32.7
Pay attention to diet	Yes	68.7	68.6	71.4
	No	31.3	31.4	28.6
Milk and/or dairy products	< 3 portions daily	90.3	91.8	90.0
	≥ 3 portions daily	9.7	8.2	10.0
	Never/ less than one day per			
Fish	week	34.9	34.1	35.1
	More	65.1	65.9	64.9
Meat	≥ 4 times weekly	39.1	34.1	33.2
	< 4 times weekly	60.9	65.9	66.8

¹ Values are self-reported and weighted except n

² Low distress (MHI-5 > 72 & ≤ 100), moderate distress (MHI-5 > 52 and ≤ 72), and high distress (MHI-5 ≤ 52)

³ ≤ 20 g ethanol daily for women, and ≤ 40 g ethanol daily for men

⁴ Hypertension and diabetes

Tab. 2: Associations between fruit and vegetable intake and psychological distress in the Swiss population (Swiss Health Survey 2102); multinomial logistic regression¹

	Total (n=20,220)				
Distress level	low	moderate		high	
		OR	95 % CI	OR	95 % CI
Vegetables/salad and/or vegetable juice (at least 3 portions per day)					
unadjusted model	1	0.87	[0.76,1.00]	0.58	[0.46,0.74]
age and sex adjusted model	1	0.81	[0.70,0.93]	0.47	[0.37,0.61]
multivariable adjusted model ²	1	0.93	[0.80,1.07]	0.64	[0.50,0.83]
multivariable adjusted model plus diet ³	1	0.93	[0.81,1.07]	0.64	[0.49,0.82]
Fruit and/or fruit juice (at least two portions per day)					
unadjusted model	1	0.84	[0.76,0.94]	0.84	[0.70,1.00]
age and sex adjusted model	1	0.80	[0.71,0.89]	0.75	[0.62,0.90]
multivariable adjusted model ²	1	0.84	[0.75,0.94]	0.85	[0.70,1.03]
multivariable adjusted model plus diet ³	1	0.83	[0.74,0.93]	0.84	[0.69,1.02]
At least 3 portions of vegetables and 2 portions of fruit per day (5-a-day)					
unadjusted model	1	0.78	[0.66,0.91]	0.50	[0.38,0.67]
age and sex adjusted model	1	0.71	[0.60,0.84]	0.41	[0.30,0.54]
multivariable adjusted model ²	1	0.82	[0.69,0.97]	0.56	[0.41,0.76]
multivariable adjusted model plus diet ³	1	0.82	[0.69,0.97]	0.55	[0.41,0.75]

¹ Weighted

² Adjusted for age, sex, nationality, smoking status, alcohol consumption, body mass index, physical activity, chronic diseases, education.

³ Adjusted for age, sex, nationality, smoking status, alcohol consumption, body mass index, physical activity, chronic diseases, education, meat consumption, fish consumption, dairy products consumption.

Chapter 1

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CHAPTER 2

Is body weight dissatisfaction a predictor of depression independent of body mass index, sex and age? Results of a cross-sectional study

Aline Richard¹, Sabine Rohrmann¹, Tina Lohse¹, Monika Eichholzer^{1,2}

¹University of Zurich; Epidemiology, Biostatistics and Prevention Institute,

Division of Chronic Disease Epidemiology; Hirschengraben 84, CH-8001 Zurich, Switzerland

²Corresponding author

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Abstract

Background: Little is known about the association of dissatisfaction with body weight - a component of body image - with depression in individuals of different sex, age, and with different body mass index (BMI). Hence, the aim of our study was to evaluate the association of body weight dissatisfaction (BWD) with depression in different sub-groups.

Methods: We analyzed data of 15,975 individuals from the cross-sectional 2012 Swiss Health Survey. Participants were asked about their body weight satisfaction. The validated Patient Health Questionnaire (PHQ-9) was used to ascertain depression. Age was stratified into three groups (18 to 29, 30 to 59, and ≥ 60 years). The body mass index (BMI) was calculated from self-reported body height and weight and categorized into underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25.0-29.9 kg/m²), and obesity (BMI ≥ 30 kg/m²). The association between body weight dissatisfaction (BWD) and depression was assessed with logistic regression analyses and odds ratios (OR) with 95% confidence intervals (CI) were computed.

Results: BWD was associated with depression in the overall group (OR 2.04, 95%CI 1.66-2.50) as well as in men (OR 1.85, 95%CI 1.34-2.56) and women (OR 2.25, 95%CI 1.71-2.96) independent of BMI. The stratification by age groups showed significant associations of BWD with depression in young (OR 1.78, 1.16- 95%CI 2.74), middle-aged (OR 2.10, 1.61- 95%CI 2.74) and old individuals (OR 2.34, 95%CI 1.30-4.23) independent of BMI. Stratification by BMI categories resulted in statistically significant positive associations of BWD and depression in underweight, normal weight, overweight and obese individuals.

Conclusion: BWD was associated with depression independent of BMI, sex and age.

Background

Body image is a complex concept that embraces numerous components including feelings, attitudes, perceptions, and behaviors toward one's body (Cash and Pruzinsky, 1990, Blashill and Wilhelm, 2014). In Western countries, research concentrated on the body's appearance, especially on body shape and body weight (Tiggemann, 2004), which is a component of body image (Forrester-Knauss and Zemp Stutz, 2012). Body image (Fallon et al., 2014) and body weight dissatisfaction (BWD) (von Lengerke et al., 2012) are very common in adolescents and adults. A German study showed that 48% of 25 to 74 year old women and 33.2% of men of the same age were affected by body weight dissatisfaction (von Lengerke et al., 2012).

An increasing number of studies indicate the importance of a healthy body image, particularly in association with eating disorders (Stice and Shaw, 2002), but also in the context of mental health and depression (Jackson et al., 2014). Depression is an important public health problem worldwide (Murray and Lopez, 1997). According to the World Health Organization, it accounts for 4.3% of the global burden of disease and is an important cause of disability worldwide (11% of all years lived with disability) (WHO, 2013a). Thus, it is of great importance to reveal risk and protective factors for this multifactorial disease.

Research on the association between various components of body image and depression has focused on adolescents (Chen et al., 2015, Ferreiro et al., 2014). In a 4-year prospective study among female adolescents, body dissatisfaction, dietary restraint, and bulimic symptoms at study entry predicted the development of major depression among initially not depressed individuals (Stice et al., 2000). Body dissatisfaction was significantly related to depression in the bivariate but not in the multivariate analysis. The evidence for an association between various components of body image and depression of female adolescents is based on a number of studies (Paxton et al., 2006, Ferreiro et al., 2012), whereas the literature is rather limited for males (Ferreiro et al., 2014).

In addition, much less is known about this association in adult males and females of different age groups (Jackson et al., 2014, Pimenta et al., 2009, Masheb and Grilo, 2003). Not all subgroups of a population may have the same psychological functioning (Chen et al., 2015, Schulte and Thomas, 2013). Furthermore, the association between body image and BWD and depression may not only depend on sex and age, but also on one's own body weight (Tang et al., 2010).

Obese individuals are frequently exposed to stigma, which can lead to poor psychological outcomes (Puhl and Heuer, 2009), such as lower self-esteem and depression (Ferreiro et al., 2014). In the present study, we aimed to evaluate the association of BWD with depression overall, in men and women, as well as in young, middle-aged and old individuals taking into account body weight. We used data of the 2012 Swiss Health Survey, a population-based representative sample of the adult population living in Switzerland.

Methods

Participants and data

We used data from the Swiss Health Survey (SHS) 2012, which was conducted by the Swiss Federal Statistical Office (SFSO) (Legal basis: Ordinance of the Conduct of Federal Statistical Surveys of 20 June 1993). The SHS does not require formal approval by an ethics committee. It is a population-based cross-sectional study, aiming to collect information about health status, several lifestyle and demographic factors, and healthcare use over time. The SHS was carried out every 5 years since 1992. Participants were selected based on registries of inhabitants using a stratified random sampling technique. In the SHS 2012, a total of 21,597 individuals aged 15 years or older and living in a private household participated. This corresponds to a response rate of 54%. Besides a computer-assisted telephone interview, a written questionnaire was provided (paper or online) upon approval from the participants (n=18,357). The multistage probability sampling and the appropriate weighting factors provided by the SFSO ensures the representativeness of the Swiss population.

Data on depression was obtained from the written questionnaire and 16,980 individuals provided information on depression status. After excluding adolescents (< 18 years; n=16,349), pregnant women (n=130) as well as individuals with missing information on body mass index (BMI) (n=90) and on body weight satisfaction (n=20) our sample consisted of 16,109 individuals. In a further step, all individuals with missing information on confounders were excluded, resulting in a final sample of 15,975 individuals.

Measurements

BWD was assessed by one question in the telephone interview asking if one is satisfied with his/her body weight. Answers were categorized into “absolutely satisfied”, “rather satisfied”,

“rather unsatisfied”, and “absolutely unsatisfied”. We then dichotomized these answers into “satisfied” and “unsatisfied” with body weight.

Depression status was considered as the outcome of our analysis. In the 2012 SHS, depression was assessed in the written questionnaire with the Patient Health Questionnaire (PHQ-9). This short screening questionnaire is a valid tool to assess depression by scoring on each of the 9 DSM-IV criteria for major depressive episodes and is broadly used in both practice and research (Kroenke et al., 2005, Manea et al., 2012). From a possible total score of 27 the cut-off point of ≥ 10 has shown a sensitivity of 88% and a specificity of 88% for the diagnosis of current major depression (Kroenke et al., 2005, Manea et al., 2012). Thus, we dichotomized a participant's PHQ-9 score into < 10 (no depression) and ≥ 10 (depression).

Potential confounders in our analyses were self-reported weight and height. BMI was calculated as weight in kg divided by squared height in meter and was categorized into underweight (BMI $< 18.5 \text{ kg/m}^2$), normal weight (BMI $18.5\text{--}24.9 \text{ kg/m}^2$), overweight (BMI $25.0\text{--}29.9 \text{ kg/m}^2$), and obesity (BMI $\geq 30 \text{ kg/m}^2$). Additional self-reported data of the participants were obtained on sex, age, area of residence (urban, rural), nationality (Swiss, non-Swiss), educational level (low [compulsory education or less] vs. middle [secondary education] vs. high [tertiary education]), marital status (married/registered partnership vs. single, divorced/dissolved, separated, widowed), smoking status (never, former, current), chronic alcohol consumption associated with health (women $\geq 20 \text{ g}$, men $\geq 40 \text{ g}$ ethanol daily vs. less), physical activity (≥ 150 minutes per week vs. less) (Bundesamt für Sport BASPO et al., 2013), paying attention to diet (yes vs. no), and self-perceived health status (fair, poor, very poor vs. very good, good) was assessed.

Statistical analyses

Analyses were conducted with the Stata statistical software version 13.1 (College Station, TX) and weighted with weighting factors according the Swiss general population. The weights are based on the 2012 Swiss population with respect to sex, age, geographic region and nationality (Swiss/non-Swiss); any differences caused by stratification or non-participation were mathematically corrected. For descriptive statistics, we present means and percentages. Logistic regression analyses examined the associations of BWD with depression (yes/no), and odds ratios (OR) with the corresponding 95% confidence intervals (CI) were calculated. We computed 4 models successively: 1) unadjusted, 2) adjusted for age

and sex, 3) adjusted for confounders chosen a priori, due to the known literature or the expected association with both, BWD and depression, except for BMI, and 4) adjusted for all the covariates in model 3 plus BMI. We used the Wald-test - including the interaction term of BWD with age, sex or BMI - to examine whether age, sex and BMI modulated the association of BWD with depression. $P < 0.05$ was considered to be statistically significant.

Results

Table 1 shows the selected characteristics of the weighted study population (mean age 47.7 years). Nearly one third (31.3%) were overweight and 10% were obese. Normal weight was reported by 56.0% of individuals and underweight by 3%. Most participants lived in urban areas (73.4%), were Swiss (80.8%), and had a middle educational level (56.5%). More than half of the participants (53.8%) were married or lived in a registered partnership. Current smoking was stated by 27.7% of the study participants and chronic hazardous alcohol consumption by 4.8%. Not reaching the recommendations for physical activity was reported by approximately one fourth (25.8%), and not paying attention to diet by 29.8% of the participants. Self-perceived health was considered as fair, poor or very poor by 14.2% of the participating individuals. Overall, 6% of the study participants were above the cut-off point of the PHQ-9, indicating a current major depressive disorder.

Barely one third (32.5%) of the study participants were absolutely satisfied with their body weight, 43.6% partly, 19.1% rather unsatisfied and 4.9% absolutely unsatisfied. As Figure 1 shows, women across all age groups were more often unsatisfied with their body weight than men. In males and females, the highest peaks of BWD were reached in 35 to 65 years old.

As shown in Figure 2, BWD was associated with depression (men and women combined OR 2.04, 95%CI 1.66-2.50; multivariable adjusted). Table 2 presents similar results when looking at the association by sex (OR 1.85, 95%CI 1.34-2.56 for men, OR 2.25, 95%CI 1.71-2.96 for women, respectively), independent of the individual's reported BMI. But results did not differ between men and women (P -interaction = 0.13).

Stratifying by age groups showed significant associations of BWD with depression in young (OR 1.78, 95%CI 1.16-2.74), middle-aged (OR 2.1, 95%CI 1.61-2.74) and old individuals (OR

2.34, 95%CI 1.30-4.23) also independent of BMI. Statistical significance for modification by age groups was not observed (P -interaction = 0.08).

By stratifying for BMI category, we found statistically significant positive associations of BWD and depression in underweight (OR 5.2, 95%CI 1.77-15.26), normal weight (OR 1.89, 95%CI 1.39-2.59), overweight (OR 2.0, 95%CI 1.41-2.83), and obese individuals (OR 1.97, 95%CI 1.10-3.51). We did not observe any statistically significant effect modification by BMI categories (P -interaction = 0.97).

Discussion

Based on data of the 2012 Swiss Health Survey, the present analyses revealed positive associations between BWD and depression independent of sex, age and BMI. To our knowledge, this is the first time these associations are studied in Switzerland.

Depression is the most common psychiatric disease in Switzerland. In the present study, 6% were affected by a major depressive disorder according to the PHQ-9. Our estimate is in line with the estimated prevalence of 6.9% in the European Union (Wittchen et al., 2011).

BWD is affecting nearly one fourth of the population living in Switzerland. The highest peaks were observed in middle-aged, 35 to 60 year olds. This is much less than what was found in a cross-sectional population-based German study (von Lengerke et al., 2012), in which body weight dissatisfaction was reported by 40% of the 25 to 74 year old men and women. However, body weight dissatisfaction was not assessed in the same way as in the SHS, which may have resulted in the observed difference.

The observed association between BWD and depression in the present study is in accordance with findings from surveys conducted mainly in adolescents and looking at the associations of various components of body image with depression (Daniels, 2005, Tang et al., 2010, Ting et al., 2012, Blashill and Wilhelm, 2014, Bearman and Stice, 2008, Almeida et al., 2012). In a U.S. study (Blashill and Wilhelm, 2014) on 2,139 adolescent males who were followed into adulthood, boys who had an average weight and perceived themselves as overweight or very underweight stated significantly more depressive symptoms than boys without body weight distortions. This result did not change over the 13-year follow-up period. In another longitudinal study among US adolescents body dissatisfaction was a

predictor of depression for females but not for males (Bearman and Stice, 2008). In a cross-sectional study among Portuguese adolescents (Almeida et al., 2012) on the other hand, body dissatisfaction contributed to depressive symptoms, without gender differences.

But in general women tend to internalize a thin appearance ideal (Thompson and Stice, 2001), whereas the ideal male body is one of lean muscularity (McCreary and Saucier, 2009, Blashill and Wilhelm, 2014). Thus, our question on body weight satisfaction may not be precise enough to distinguish between obesity and muscularity. Since both obesity and muscularity dissatisfaction are of importance of the masculine body image upcoming research should assess both of them (Blashill and Wilhelm, 2014). Although sex did not modulate the associations between BWD and depression, women tended to be more often dissatisfied than men.

In adults, the evidence is limited and not yet conclusive (Jackson et al., 2014, Gaskin et al., 2013, Fallon et al., 2014, Masheb and Grilo, 2003, Pimenta et al., 2009). A cross-sectional analysis of the American Study of Women's Health Across the Nation (SWAN) (Jackson et al., 2014) observed that middle-aged women with body image dissatisfaction or who perceived themselves as "unattractive", but not those with BWD, were more likely to report clinically significant levels of depressive symptoms. Also in a study conducted with 97 mainly female U.S. patients with binge eating disorders, body image disturbance was positively associated with depression (Masheb and Grilo, 2003). In contrast, a prospective survey among Spanish university graduates, showed no association between body image disturbance and subsequent depression neither in adult men nor in adult women (Pimenta et al., 2009).

Others investigated whether body weight categories may modulate the association between BWD and depression. A variety of studies conducted with children or adolescents observed that perception of body weight may be more important than objectively measured weight in the relationship with mental health, e.g. with suicide ideation or attempts (Armstrong et al., 2014, Gray et al., 2012, Ali et al., 2010, Eaton et al., 2005). Furthermore, in a cross-sectional Chinese Study (Tang et al., 2010) adolescents who perceived themselves as overweight were more likely to experience depressive symptoms than those who perceived themselves as normal and/or underweight. In the same study, no significant association between depressive symptoms and actual measured weight status was observed. In a population-based cross-sectional American Study (NHANES) with over 13,000 participants, women who perceived themselves as underweight or overweight had an increased odd of depression

compared with women who perceived themselves as about the right weight. This association was independent from measured weight. Among men, perceiving oneself as underweight but not being underweight (objectively measured) was associated with depression (Gaskin et al., 2013). Accordingly, in our study, BWD remained to be associated with depression after adjustment for BMI. Thus, we confirmed the results of previous studies showing that perception of body weight might be a better predictor for depression than actual weight status.

Moreover, in our study, BWD was not only positively associated with depression in underweight, overweight and obese individuals but also in those with normal weight. Similarly, a recent cross-sectional study on Chinese adolescents looked at the moderating factors between the association of body dissatisfaction and depression. They observed significant associations in underweight, normal weight and overweight females, but in males associations were only observed in underweight and normal weight adolescents (Chen et al., 2015).

Potential mechanisms how body dissatisfaction is associated with mental health have been postulated previously (Chen et al., 2015, Tang et al., 2010), focusing on the fact that body dissatisfaction stems from an inappropriate emphasis on the importance of thinness and other unachievable standards of beauty and, thus, may affect depression onset. This hypothesis is supported by the longitudinal study from Stice et al. (Stice et al., 2000) on female adolescents, in which body dissatisfaction has been identified as a predictor of depression. In this context, experiencing weight stigma predicts poor psychological outcomes including depression, similar to those outcomes who have been linked to higher BMI (Stevens et al., 2016). On the other hand, an association between body image and depression is also supported by the findings from neurobiological investigations (Tang et al., 2010). Deficits in the hypothalamic pituitary-adrenal axis and serotonin system have been shown to be involved in mood disorders as well as in weight regulation. Furthermore, also brain areas which are involved in hedonic regulation may play a role for both body image and depression (Hoebel and Leibowitz, 1981).

Our study has several strengths, including the large, nationally representative sample of individuals 18 years and older living in Switzerland, due to the use of weighting factors, which allows for the extrapolation of the results in relation to age, sex, region and nationality from the sample to the total population. Furthermore, the survey data allowed

for adjusting for a number of important covariates associated with BWD and depression, although we were not able to take all potential confounders into consideration, such as family history of depression, medication, and also residual confounding might have occurred. A further strength was that depression was defined using a validated instrument with DSM-IV based criteria. However, our analysis was based on a cross-sectional study, and therefore we cannot exclude reverse causation, i.e. depression may also lead to BWD, which is a major limitation. Nevertheless, as these associations have not been examined yet for Switzerland, it is worthwhile to start with this population-based cross-sectional approach, but longitudinal studies are needed to examine the temporal relationship between body image and depression. Because institutionalized individuals were excluded from the sampling procedure, excluding most probably cases with severe depression, thus the prevalence of depression is possibly underestimated. The fact, that BWD, depression, body weight, height, and potential confounders were based solely on self-report may have biased the results. Finally, it should be noted that although BWD and body image dissatisfaction are related constructs, they are not redundant. The various aspects of body image and depression discussed in the present literature have therefore to be taken into consideration.

In conclusion, BWD was observed to be widespread and affected nearly one fourth of the population living in Switzerland. In this representative sample, BWD was associated with depression. The association was independent of age, sex, and BMI, i.e. present in individuals with normal body weight and in all age groups. Our results need to be confirmed in longitudinal studies. Presumed that causality can be provided in future longitudinal studies, programs that aim to reduce depression by diminishing body (weight) dissatisfaction should refer to all weight groups.

Abbreviations

BMI: Body mass index; BWD: Body weight dissatisfaction; CI: Confidence interval; OR: Odds ratio; PHQ-9: Patient Health Questionnaire; SE: standard error; SHS: Swiss Health Survey; SFSO: Swiss Federal Statistical Office.

Competing interests

The authors declare that there are no financial or personal relationships with other people or organizations that could inappropriately influence the work reported or the conclusions, implications, or opinions stated.

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Authors' contributions

AR and ME designed the study. AR performed the statistical analyses and AR and ME wrote the manuscript. All authors contributed to the interpretation of the data and edited the manuscript. ME supervised the study. All authors contributed to and have approved the final manuscript.

Availability of data and materials

Individual data of the Swiss Health Survey are property of the Swiss Federal Statistical Office (SFSO) and may only be made available by SFSO. Requests for access have to be submitted to Mr. Marco D'Angelo (head of division, MarcoDAngelo@bfs.admin.ch). For information contact sgb12@bfs.admin.ch.

Chapter 2

Tables and Figures

Fig. 1: Prevalence of body weight dissatisfaction; 2012 Swiss Health Survey

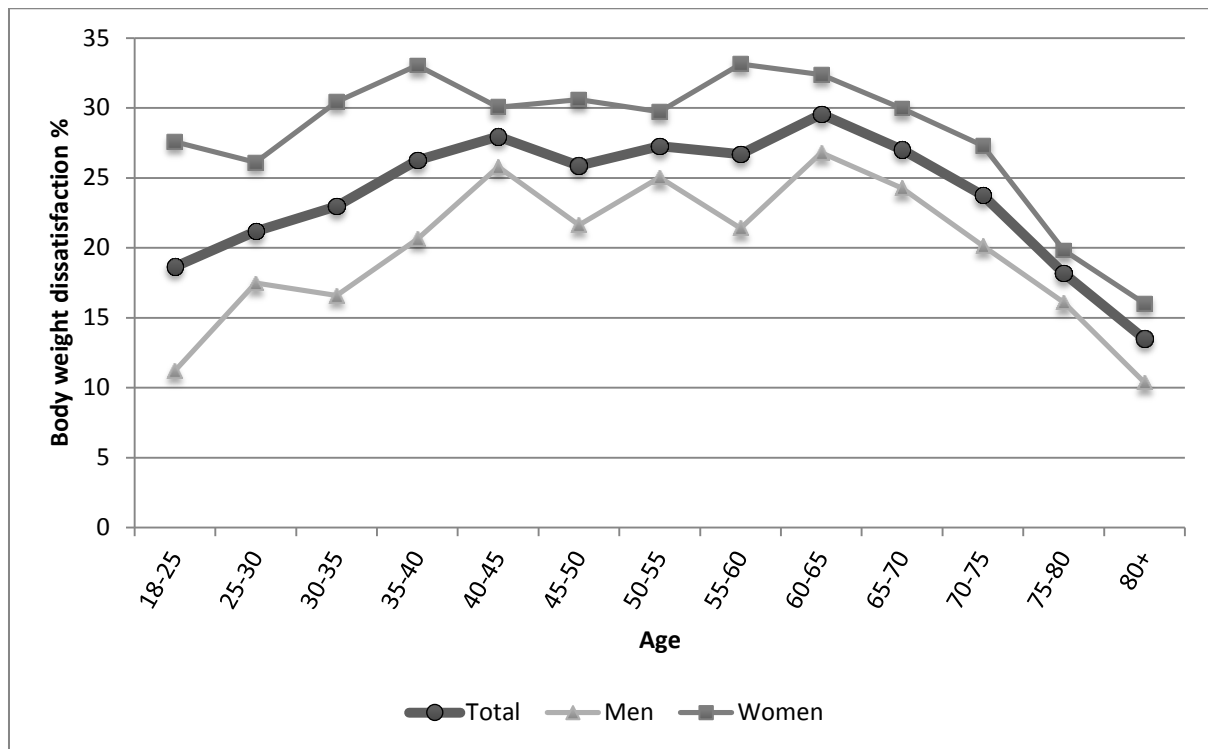


Fig. 2: Associations between body weight dissatisfaction and depression; 2012 Swiss Health Survey

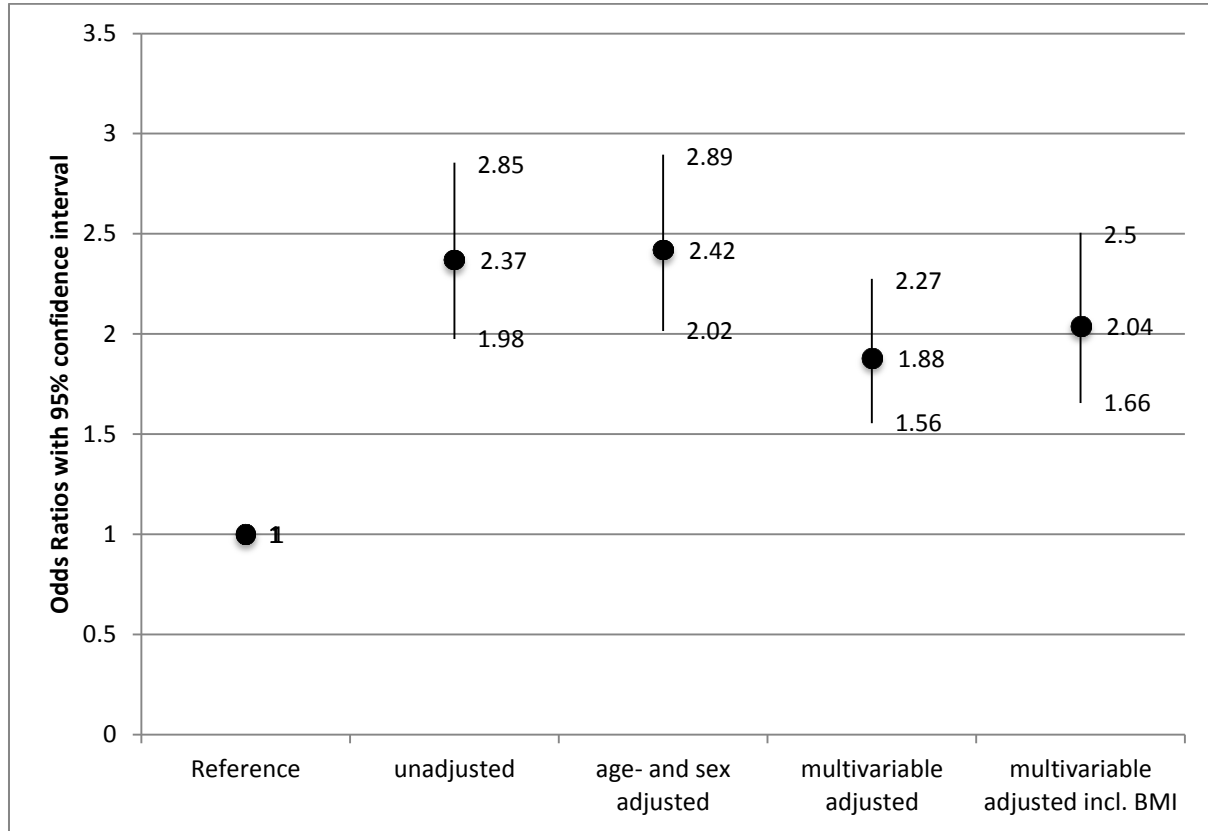


Figure legend: Associations between body weight dissatisfaction and depression assessed with logistic regression analyses and adjusted for different confounders; 2012 Swiss Health Survey. Multivariable adjustment included the variables area of residence, nationality, educational level, smoking status, physical activity, marital status, alcohol consumption, attention to diet, self-reported health, age (if appropriate), sex (if appropriate), and body mass index (if appropriate).

CHAPTER 2

Tab. 1: Characteristics of the study sample of the 2012 Swiss Health Survey¹

		Total
Total, n		15,975
Age, mean (SE)		47.7 (0.18)
Sex	Males	50.2
	Females	49.8
Body mass index (BMI)	Underweight (BMI < 18.5 kg/m ²)	3.0
	Normal weight (BMI ≥ 18.5 to < 25.0 kg/m ²)	56.0
	Overweight (BMI ≥ 25 to < 30.0 kg/m ²)	31.3
	Obesity (BMI ≥ 30 kg/m ²)	9.7
Area of residence	Urban	73.4
	Rural	26.6
Nationality	Swiss	80.8
	Foreign	19.2
Educational level	High	33.3
	Middle	56.5
	Low	10.2
Marital status	Married / registered partnership	53.8
	Single, divorced / dissolved partnership, separated, widowed	46.2
Smoking status	Never smokers	49.3
	Ex-smoker	23.0
	Current smokers	27.7
Chronic alcohol consumption ²	No	95.2
	Yes	4.8
Physical activity	≥ 150 min. per week	74.2
	< 150 min. per week	25.8
Pay attention to diet	Yes	70.2
	No	29.8
Self-perceived health	Good, very good	85.8
	Fair, poor, very poor	14.2
Body weight satisfaction	Absolutely satisfied	32.5
	Partly satisfied	43.6
	Rather unsatisfied	19.1
	Absolutely unsatisfied	4.9
Depression	No	94.0
	Yes	6.0

¹ Weighted according to the Swiss general population

² Ethanol ≥ 20 g/day for women, ≥ 40 g/day for men vs. less

CHAPTER 2

Tab. 2: Association between body weight dissatisfaction and depression stratified by sex, age and body mass index; 2012 Swiss Health Survey¹

	No depression (ref.)	unadjusted		age adjusted		multivariable adjusted ²		multivariable adjusted ² incl. BMI	
Body weight dissatisfaction	OR	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Men	1	1.89	[1.41,2.54]	2.05	[1.54,2.74]	1.60	[1.18,2.18]	1.85	[1.34,2.56]
Women	1	2.76	[2.21,3.45]	2.77	[2.21,3.47]	2.16	[1.72,2.72]	2.25	[1.71,2.96]
<i>p-Interaction</i> ³		0.01		0.09		0.18		0.13	
sex adjusted									
≥ 18 to < 30 years	1	1.91	[1.28,2.86]	1.88	[1.27,2.79]	1.53	[1.02,2.30]	1.78	[1.16,2.74]
≥ 30 to < 60 years	1	2.77	[2.22,3.45]	2.74	[2.20,3.41]	2.05	[1.62,2.59]	2.10	[1.61,2.74]
≥ 60 years	1	2.63	[1.72,4.02]	2.64	[1.71,4.08]	2.04	[1.29,3.23]	2.34	[1.30,4.23]
<i>p-Interaction</i>		<0.01		0.01		0.07		0.08	
age and sex adjusted									
Underweight (BMI < 18.5 kg/m ²)	1	5.19	[2.25,11.95]	5.17	[2.14,12.50]	5.20	[1.77,15.26]		
Normal weight (BMI ≥ 18.5 to < 25.0 kg/m ²)	1	2.52	[1.87,3.41]	2.43	[1.81,3.28]	1.89	[1.39,2.59]		
Overweight (BMI ≥ 25 to < 30.0 kg/m ²)	1	2.80	[2.02,3.89]	2.46	[1.77,3.42]	2.00	[1.41,2.83]		
Obesity (BMI ≥ 30 kg/m ²)	1	2.53	[1.41,4.54]	2.19	[1.20,3.98]	1.97	[1.10,3.51]		
<i>p-Interaction</i>		0.48		0.49		0.97			

¹Weighted according to the Swiss general population

²Adjusted for area of residence, nationality, educational level, smoking status, physical activity, marital status, alcohol consumption, attention to diet, self-reported health, age (if appropriate), sex (if appropriate), and body mass index (if appropriate)

³Interaction term: cross-product of sex, age-groups or weight groups, respectively, with body weight satisfaction

Chapter 2

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CHAPTER 3

Loneliness is adversely associated with lifestyle and physical and mental health. Results of a cross-sectional study from Switzerland

Aline Richard^{1*}, Sabine Rohrmann¹, Caroline L. Vandeleur², Margareta Schmid¹, Jürgen Barth³, Monika Eichholzer¹

¹ Epidemiology, Biostatistics and Prevention Institute, Division of Chronic Disease Epidemiology, University of Zurich, Hirschengraben 84, 8001 Zurich, Switzerland

² Centre for Research in Psychiatric Epidemiology and Psychopathology, Department of Psychiatry, University Hospital of Lausanne, Site de Cery, 1008 Prilly, Switzerland

³ Institute for Complementary and Integrative Medicine, University Hospital and University of Zurich, Sonneggstr. 6, 8091 Zurich, Switzerland

*Corresponding author

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Abstract

Background: Loneliness is a common emotional distress experience and is associated with unhealthy lifestyle and adverse physical and mental health. Nevertheless, little is known about the prevalence of loneliness in different age groups, and about age and sex as potential effect modifiers of the association between loneliness and lifestyle or health-related factors. Thus, the aim of the study was to examine the prevalence of loneliness in adults in Switzerland and to assess the associations of loneliness with several behavioral, physical and mental health factors, including the modulating effect of sex and age.

Methods: Data from 20,007 participants of the cross-sectional population-based Swiss Health Survey 2012 (SHS) were analyzed. Logistic regression analyses were used to assess associations of loneliness with lifestyle and health-related factors (e.g. physical activity, diabetes, depression). Wald tests were used to test for interactions.

Results: Loneliness was distributed in a slight U-shaped form from 15 to 75+ year olds, with a mean percentage of 64.1% who had never felt lonely. Loneliness was significantly associated with most lifestyle factors (e.g. smoking; Odds ratio [OR] 1.13, 95% confidence interval [CI] 1.05-1.23). Lonely individuals were more often affected by health-related factors, such as high cholesterol levels (OR 1.31, 95% CI 1.18-1.45), diabetes (OR 1.40, 95% CI 1.16-1.67), self-reported chronic diseases (OR 1.41, 95% CI 1.30-1.54), impaired self-perceived health (OR 1.94, 95% CI 1.74-2.16), moderate and high psychological distress (OR 3.74, 95% CI 3.37-4.16), and depression (OR 2.78, 95% CI 2.22-3.48). We observed effect modification by age, but not by sex.

Conclusion: Loneliness is associated with unhealthy lifestyle and poorer physical and mental health, modulated by age, not by sex. Our findings illustrate the importance of considering loneliness for lifestyle and health factors, not only in older, but also in younger and middle-aged adults. Longitudinal studies are needed for Switzerland to elucidate the causal relationships of these associations.

Background

Throughout decades loneliness has commonly been described by philosophers, psychologists and in the literature as ubiquitous and even as an essence of human being [1]. The felt sense of loneliness as an emotional distress experience with a perception of unsatisfying social relationships is a key element of the definition of loneliness. Perceived unsatisfying relationships, thus, are independent of the quantity of social interactions, but are caused by the felt sense of social isolation and unsatisfied need for affection in current relationships [2, 3]. Nevertheless, a low quantity and meaning of social contacts has also been related to loneliness [4-7].

Sociodemographic characteristics are partly associated with loneliness. In general women seem to report loneliness more frequently than men [8, 9], although the gender differences may disappear when controlling for other factors [4]. For age some authors described a U-shaped prevalence with more lonely subjects in younger and older adults than in middle age [3, 10]. However, other authors suggested that loneliness is more common in older age [11-14]. Overall, most studies focused on older age [4, 15-21] and little is known about the prevalence of loneliness in younger age groups [22, 23].

Other demographic factors have been suggested as risk factors for loneliness, such as being single and/or living alone [10, 22, 24], low educational and low-income levels [15, 25, 26], and immigration status, especially immigration in women [27]. In contrast, whether living in an urban or rural area is associated with loneliness still yields contradictory results [15, 25, 28].

Loneliness can be a transient state, but more important it can be also a long-lasting perception with negative behavioral and health outcomes [29, 30]. Loneliness is associated with increased morbidity and mortality risk [18, 31] and it is associated with a lower capacity for self-regulation [3]. In consequence less self-regulation goes along with worse lifestyle: Lonely individuals are less physically active [32], are more often affected by alcohol abuse [33] and are more often obese [34] than non-lonely persons. Consequently, there is increasing evidence that lonely individuals feel less healthy [35], have a higher risk for hypertension [36], hypercholesterolemia, the metabolic syndrome [18], and coronary heart disease [37]. Furthermore, loneliness has been related to mental health problems, such as psychosis [38, 39], suicide [40], and depression [3, 41].

In 2011, a study compared loneliness in 25 European countries and a north-south gradient for self-reported frequent loneliness in Europe was observed. In Northern Europe, including Switzerland, loneliness was under 6 %, in contrast to higher prevalence in Southern Europe [14]. To have an population-based estimate of loneliness frequency and due to the fact that most studies looking at the associations of loneliness with health stem from North American cohorts [3], it is worthwhile to investigate the prevalence as well as the associations of loneliness with health and lifestyle for Switzerland. In Switzerland, the evidence for the associations of loneliness with lifestyle and health is very limited. One study found strong associations of loneliness with major depressive episode [42, 43]. Nevertheless, nothing is known about further lifestyle and health outcomes for Switzerland.

Against this background, we aimed to determine the prevalence of loneliness in a large representative sample of the Swiss population aged 15 years and older, to evaluate loneliness and its associations with lifestyle and health outcomes, with a special emphasis on whether sex and age modulate these associations.

Methods

Study population and data

Data were obtained from the Swiss Health Survey (SHS) conducted in 2012/2013 by the Swiss Federal Bureau of Statistics (SFSO) (Legal basis: Ordinance of the Conduct of Federal Statistical Surveys of 30 June 1993). This cross-sectional, population-based nationwide survey focuses on health status, several lifestyle and demographic factors, and healthcare use and has been carried out every five years since 1992. It uses a stratified random sampling technique based on registries of inhabitants. Out of an initial sample of 41,008 individuals a total number of 21,597 individuals aged 15 years or older and living in a private household agreed to participate in the 2012 SHS (i.e. participation rate 54%). They participated in a computer-assisted telephone interview (CATI). In the next step, a written questionnaire was provided (paper or online) upon approval from the participants (n=18,357). The representativeness of the Swiss population was determined by the multistage probability sampling and the appropriate weighting factors provided by the SFSO.

From the telephone interview 20,841 individuals had available information on loneliness status. After excluding individuals with missing information on health outcomes (according

to table 1) data on 20,405 individuals were available. In a further step, we excluded individuals with missing information on lifestyle ($n=398$), and our final sample therefore consisted of $n=20,007$ individuals. Depression was only assessed in the written questionnaire ($n=18,375$), and thus, we could finally include 16,114 individuals with sufficient information on depression status in our analysis considering depression.

Measurements

Loneliness was used as a predictor variable and assessed by one item asking the participants how often they felt lonely. Answers were dichotomized into never vs. sometimes, quite often and very often.

Outcome variables were divided into two parts, first into lifestyle, and second, into health-related factors. Lifestyle included smoking status (never and former vs. current), chronic alcohol consumption associated with a health risk (women ≥ 20 g, men ≥ 40 g ethanol daily vs. less), binge drinking (≥ 6 glasses of alcohol at one occasion within the last year vs. less often), physical activity (≥ 150 minutes per week vs. less) [44], paying attention to diet (yes vs. no), keeping to the 5-a-day recommendation of fruit and vegetable consumption according to the recommendations of the Swiss Society for Nutrition [45] (yes vs. no) and having visited a medical doctor within the last year (yes vs. no). Risk factors for cardiovascular diseases were assessed as health outcomes: body mass index (BMI) dichotomized into overweight and obese ($\text{BMI} \geq 25.0 \text{ kg/m}^2$) vs. less. For adolescents aged 15 to 18 years tables of Cole were used to define overweight and obesity [46]. Further health outcomes were self-reported diagnoses of diabetes, hypertension and high cholesterol concentration (yes vs. no), self-reported non specified chronic diseases (self-reported ongoing disease or health problem lasting for at least 6 months or expected to last further than 6 months vs. none), self-perceived health (good and very good vs. fair, poor and very poor), and psychological distress (low vs. moderate and high) during the previous 4 weeks (assessed by the 5-item mental health index [MHI-5] [47]. From the written questionnaire the validated Patient Health Questionnaire (PHQ-9) was used to detect depression (yes vs. no). We used a cut-off point of ≥ 10 vs. less, which has been shown to have a sensitivity of 88% and a specificity of 88% for the diagnosis of major depression [48, 49].

Confounders were chosen a priori due to the known literature and included sex, age, area of residence (urban vs. rural), nationality (Swiss vs. non-Swiss), educational level (low:

compulsory education or less vs. middle: secondary education vs. high: tertiary education), marital status (married/registered partnership vs. single, divorced/dissolved, separated, widowed), household size (living alone vs. not living alone), and social support (high, middle, low; based on the Oslo-3-social support scale [50]).

Statistical analyses

All statistical analyses were conducted using STATA software version 13.1 (College Station, Texas). Weighted percentages were used to illustrate the prevalence of loneliness, socio-demographics, lifestyle and health outcomes. The prevalence of loneliness was shown in 5-year age groups. For further analyses three age groups (15-29, 30-59, and 60+ years) were built.

Logistic regression analyses were used to determine associations of loneliness with lifestyle and health outcomes in three models (model 1 unadjusted, model 2 age- and sex adjusted, and model 3 adjusted for age, sex, area of residence, nationality, educational level, marital status, household size, and social support). Odds ratios (OR) with the corresponding 95% confidence intervals (95% CI) were computed. Sampling weights, provided by the SFSO, were used for all analyses which allows for comparison with the permanent 2012 Swiss population regarding sex, age, geographic region and nationality (Swiss vs. non-Swiss). Furthermore, a sub-analyses with loneliness dichotomized in its extreme groups (feeling never vs. quite/very often lonely) was performed and associations of this modified loneliness with lifestyle and health outcomes were analyzed.

The Wald test was used to examine whether the associations of loneliness with indicators of lifestyle, physical and mental health were modified by age and sex.

Results

Characteristics of the sample are provided in Table 1. Approximately two thirds (64.1%) reported never feeling lonely, whereas feeling lonely “sometimes”, “quite often” or “very often” was expressed by 31.7%, 2.7% and 1.5% of the study participants, respectively. A description of the perceived frequency of loneliness in 5-year age steps from 15 to 80 years or older is shown in Figure 1. In all age groups there were between 26% and 47% of individuals who felt sometimes, quite or very often lonely. Furthermore, feeling lonely was

reported more often by younger individuals than by older ones, with a peak at around 25 to 29 years of age, and a decrease from 70 to 74 years of age followed by a small increase thereafter (Fig. 1).

Table 2 shows the multivariable adjusted associations between loneliness and lifestyle and health outcomes. Compared to participants who never felt lonely, lonely men and women were statistically significantly more frequently current smokers (OR 1.13, 95% CI 1.05-1.23), less physically active (OR 1.20, 95% CI 1.10-1.31), and adhering less often to the 5-a-day recommendations (OR 1.21, 95% CI 1.07-1.37) (Table 2, multivariable adjusted for sociodemographic and social support variables in table 1). Loneliness was not associated with chronic alcohol consumption, binge drinking, or paying attention to diet.

Loneliness was statistically significantly associated with high cholesterol concentration (OR 1.31, 95% CI 1.18-1.45), diabetes (OR 1.40, 95% CI 1.16-1.67), self-reported chronic diseases (OR 1.41, 95% CI 1.30-1.54), impaired self-perceived health (OR 1.94, 95% CI 1.74-2.16), with having more often contact with physicians during the past 12 months (OR 1.29, 95% CI 1.17-1.42), moderate and high psychological distress (OR 3.74, 95% CI 3.37-4.16), and depression (OR 2.78, 95% CI 2.22-3.48) (Table 2, multivariable adjusted). No associations were observed between loneliness and BMI and loneliness and hypertension.

We only observed one statistically significant interaction of loneliness with sex, for paying attention to diet (p -interaction < 0.001, data not shown). Indeed, lonely men paid statistically significantly more often attention to diet than men who never felt lonely, but there was no such an association between loneliness and diet in women.

Associations were even stronger in the sub-analysis, in which never lonely individuals were compared to quite and very often lonely individuals, with one exception, such as the association of loneliness with smoking was no longer statistically significant (data not shown).

Table 3 shows the multivariable adjusted associations between loneliness and lifestyle and health outcomes, stratified by age group. We observed statistically significant effect modification by age group and loneliness for BMI, smoking, visiting a physician within the past year, and self-perceived health, but not for any other lifestyle or health characteristic (all other p -interactions ≥ 0.05 ; data not shown). Loneliness was not statistically significantly associated with BMI for the total sample, but younger lonely participants (up to 59 years)

tended to have lower odds of being overweight or obese than older participants (Table 3). Lonely 15 to 29 and 30 to 59 year old subjects were statistically significantly more often ever or current smokers than subjects who never felt lonely. In the oldest age group, loneliness was most strongly associated with visits to a physician within the past year, followed by the middle-aged group. The association of loneliness with self-perceived health was strongest in the 30 to 59 year age group but was also statistically significant in 15 to 29 year old subjects as well as in subjects aged 60 years or older.

Discussion

One third of the Swiss population report to feel lonely to some extent and about five percent claim to feel often or very often lonely. Loneliness is more prevalent in young adults and in individuals older than 75 years, which confirmed the hypothesis of a U-shaped association over the life course of earlier studies [3, 14]. However, as observed by Heinrich and Gullone [29] many studies on the prevalence of loneliness are not up to date.

Loneliness and lifestyle factors

In the Swiss population, feeling lonely was associated with smoking, physical inactivity, and non-adherence to the 5-a-day recommendation. Sex did not – with one exception - modulate these associations. Age, on the other hand, had a modulating effect for high BMI and smoking.

For smoking our results are in line with a newer systematic review, which found half significant and another half non-significant associations of loneliness and smoking, with one exception [51]. In our study, lonely young (15 to 29 year old) and middle-aged (30 to 59 year old) participants, but not those of 60 years and older, smoked more often than participants who did not feel lonely. As DeWall and Pond [52] pointed out, young individuals may start smoking in an attempt to connect with others and gain social acceptance.

We observed no association between loneliness and neither chronic alcohol consumption nor binge drinking. A population-based study in the US found an association of loneliness with reduced alcohol use, and not with binge drinking in individuals of 50 years or older [53]. In contrast, loneliness was considered to be a contributing, maintaining and poor prognostic factor in the development of alcohol abuse and a risk factor for all stages of alcoholism in a

recent review [54]. A recent study tried to explain these inconsistent findings by assessing transient loneliness and individual drinking behaviors, revealing that loneliness was related to an increase in solitary consumption and a decrease in social alcohol consumption [55].

To our knowledge, no study had yet examined the association of loneliness with physical activity in the age range of total adulthood. We observed an association between loneliness and physical inactivity, independently of age. Hence, our findings are in accordance with previous literature on older adults, such as an Israeli study with a random sample [56] and a Canadian longitudinal study [57], in which loneliness was associated with a lower odds of engaging in physical activity. Similarly, in the study of Hawkey et al. [32] loneliness was an independent risk factor for physical inactivity among adults aged 50 years and above. As loneliness was associated with poor emotional self-regulation [3], lonely people may exhibit higher levels of negative affect than socially connected people, which may contribute to reduced motivation to engage in physical activity. Further studies, especially with samples of younger individuals, are needed to elucidate these associations.

We observed no overall association between feeling lonely and attention to diet, but lonely men did pay attention more often to their diet than male participants who did not feel lonely. Adherence to the 5-a-day recommendation of fruit and vegetable consumption, on the other hand, which can be interpreted as a proxy for “healthy” diet [45], was reported less frequently among lonely individuals. To our knowledge the association of loneliness with healthy or unhealthy diet has scarcely been examined, with the exception of the effect of loneliness on malnutrition in the elderly [58] and in relation to eating disorders [59, 60]. However, our data were too limited to further evaluate these associations.

Loneliness and physical and mental health

Participants who felt lonely were significantly more likely to report poor self-rated health, visits to medical doctors, hypercholesterolemia, diabetes, chronic diseases, distress, and depression than participants who did not feel lonely.

In contrast to some [20, 36] but not all other studies [61], we observed no associations between loneliness and hypertension. Loneliness was associated with higher total peripheral resistance in a study of young adults [62], a mechanism by which loneliness may contribute to the development of hypertension [61].

There is also evidence from the literature of a positive association between loneliness and overweight, obesity and central obesity. Accordingly, in a cross-sectional study on 1289 adults in Australia a higher proportion of lonely than non-lonely individuals were overweight and obese [34]. In a population-based study in England loneliness was associated with an increased likelihood for meeting criteria of the metabolic syndrome and with the individual criteria of central obesity and elevated fasting blood glucose, but not of high blood pressure and dyslipidemia [18]. Higher food consumption might partially explain the latter associations [18, 61, 63]. It was hypothesized by Jaremka et al. [64] that loneliness might predict higher post-prandial ghrelin concentration and hunger in women with a lower BMI. Ghrelin, a hormone which increases appetite, may thus link loneliness to weight gain. This association was not confirmed in the present study. There was no overall association between loneliness and BMI, although the association was modulated by age pointing towards a tendency for lower odds of overweight and obesity in lonely younger but not in older participants.

In the present study, lonely individuals also visited a medical doctor more often during the past year than participants who did not feel lonely. This association was observed in middle-aged and older but not in younger individuals, which confirms results of previous studies [65-67]. Ellaway et al. [67] concluded that medical doctors possibly fulfill a social role for those who need someone to talk to.

In several other studies loneliness was associated with poor self-rated health [15, 23, 25, 68]. In a longitudinal study in Finland, never or seldom feeling lonely predicted good self-rated health over time [35]. The association was stronger among women than among men. The authors of the study hypothesized that among men voluntarily work and the associated social support might reflect pathways between loneliness and self-reported health. Among women, the initial significant association disappeared after adjusting for baseline health conditions. In our study, the association was not modulated by sex but it was by age. Even though a significant association was observed in all three age groups, the association of loneliness with self-perceived health was surprisingly strongest in 30 to 59 year olds.

Besides self-reported health, lonely individuals in this study also reported being affected by chronic diseases more often than individuals who did not feel lonely. Whether the report of chronic diseases is elevated in lonely people or whether chronic diseases are indeed more frequent in lonely people is not obvious, due to the single item question about ongoing

diseases or health problems lasting for at least 6 months or expected to last further than 6 months. Lonely individuals may recall or estimate information differently than not lonely people [69]. Nevertheless, other studies also revealed a positive association of loneliness with chronic diseases [15, 70].

Loneliness was also associated with psychological distress and depression in the present analysis. Indeed, we observed a strong association of loneliness with psychological distress, assessed by the MHI-5. The MHI-5 has been shown to be a valid tool to detect depression in the general population and in psychiatric surveys [47, 71, 72]. Other studies found similar results, going into even more detail, such as the finding that the association of loneliness with distress depended on the duration of experienced loneliness or that associations were only observed in specific dimensions of distress [73-75]. Furthermore, depression has often been described to be accompanied by loneliness, but loneliness does not inevitably end in depression. Thus, loneliness may be both, a risk factor for or a consequence of depression. Our results are in line with those of other studies that found positive associations between loneliness and depression [41, 76, 77]. Although there are not only cross-sectional but also longitudinal studies that found an increased risk of depression with precedent loneliness, only older adults were included in these samples [41, 78, 79]. To our knowledge, besides one older study that included undergraduate students aged 21 or above [80], no study had assessed loneliness and depression among younger adults. Thus, our results contribute to a better awareness of an underestimated health risk factor for all ages, and not only among older adults.

Strength and limitations

The major strengths of our study are, first, that the associations of loneliness with various health-related factors were examined, and, second, that we included all the adults in this population-based survey, stratifying them by age. Research on these associations, especially with behavioral factors, is still rare and only scarce research exists for younger adults. Furthermore, we tested for age and sex interaction, which has rarely been evaluated before [6, 10]. Unfortunately, we could not analyze the adolescents separately because of the limited number, and thus, included them in the group of younger adults.

A further strength is the use of a validated scale for depression and psychological distress, as well as the multivariable adjustment, which includes adjustment for social support. Last but

not least, our study is representative of the Swiss population, although individuals living in institutions (e.g. nursing homes, hospital, prisons) were not included and thus, we missed a group of individuals with worse health, which are more frequent in older age groups.

Results of our study also entail several limitations. First, we were limited by the cross-sectional study design. No causal conclusions could be derived since the direction of the associations cannot be determined. Thus, it is difficult to determine whether loneliness followed exposure in time or exposure resulted from loneliness. However, our results support prospective studies and are in line with theoretical frameworks on the association of loneliness and health. Due to the lack of longitudinal data in Switzerland and the limited research on loneliness and its overall consequences, it is worthwhile to present population-based cross-sectional data. A further limitation is that the study was based on self-reported data, assessed only once. Inaccurate self-reporting can be caused by recall bias, social desirability bias and errors in self-observation. There might also be a bias in regard to a healthy participant effect in the Swiss Health Survey.

In the present study, loneliness was assessed by one single question which included the word “lonely”. As a consequence of this phenomenological approach participants may have understood loneliness in different ways. Moreover, the use of a direct single-item question which included the word “lonely” may have resulted in under-reporting due to the social stigma of loneliness. But these single-items questions were validated by a comparison with the validated UCLA Loneliness Scale [22].

Conclusion

Loneliness was apparent throughout the total age range of adulthood and was associated with unhealthy behavior and poorer physical and mental health. Furthermore, loneliness was modulated by age, but not sex (with one exception), for some but not all health factors. Our findings illustrate the importance of considering loneliness for lifestyle and health factors, not only in older, but also in younger and middle-aged adults. Due to our cross-sectional study design no causal relationship could be inferred and, thus, evaluating loneliness in a longitudinal perspective is needed to contribute to a better understanding of the importance of loneliness as an independent risk factor for physical and mental health for Switzerland.

Abbreviations

BMI: Body mass index; CI: Confidence interval; OR: Odds ratio; PHQ-9: Patient Health Questionnaire; SHS: Swiss Health Survey; SFSO: Swiss Federal Statistical Office.

Competing interests

The authors declare that there are no financial or personal relationships with other people or organizations that could inappropriately influence the work reported or the conclusions, implications, or opinions stated.

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Authors' contributions

AR and ME designed the study. AR wrote the manuscript and performed the statistical analyses. All authors contributed to the interpretation of the data and edited the manuscript. ME supervised the study. All authors contributed to and have approved the final manuscript.

Availability of data and materials

Individual data of the Swiss Health Survey are property of the Swiss Federal Statistical Office (SFSO) and may only be made available by SFSO. Requests for access have to be submitted to Mr. Marco D'Angelo (head of division, MarcoDAngelo@bfs.admin.ch). For information contact sgb12@bfs.admin.ch.

Ethical Standards

The data collection and data storage for the Swiss Health Survey (Schweizerische Gesundheitsbefragung) does not require formal approval by an ethical committee. This data collection is specifically permitted under Swiss law (SR 431.012.1 and SR 431.112.1). Individuals invited to participate received a brief description of the study and could decline to participate or withdraw at any time. Participants' responses were treated confidentially and aggregated anonymous responses were utilized for analyses presented herein.

Chapter 3

Tables and Figures

CHAPTER 3

Tab. 1: Characteristics of the study sample of the 2012 Swiss Health Survey¹

		Total
Total, n		20,007
Age, mean (SE)		47 (0.17)
		%
Socio-demographics		
Sex	Males	49.1
	Females	50.9
Age (years)	≥ 15 to < 30	21.1
	≥ 30 to < 40	15.9
	≥ 40 to < 50	20.3
	≥ 50 to < 60	15.8
	≥ 60 to < 70	13.2
	≥ 70	13.7
Area of residence	Urban	72.9
	Rural	27.1
Nationality	Swiss	78.9
	Non-Swiss	21.1
Educational level	High	29.7
	Middle	54.4
	Low	16.0
Marital status	Married / registered partnership	51.0
	Single, divorced / dissolved partnership, separated, widowed	49.0
	Living alone	13.2
Household size	High	45.2
Social support	Middle	49.7
	Low	1.2
	Don't know / no answer	3.9
Lifestyle factors		
Smoking status	Never smokers	49.9
	Ex-smoker	21.7
	Current smokers	28.4
Chronic alcohol consumption ²	No	95.2
	Yes	4.8
Binge drinking (6 glasses or more on one occasion)	No (less than 1 time per year)	66.7
	Yes (more than 1 time per year)	33.3
Physical activity	≥ 150 min. per week	73.0
	< 150 min. per week	27.0
Pay attention to diet	Yes	69.0
	No	31.0
Adherence to the 5-a-day recommendation	Yes	11.1
	No	88.9

CHAPTER 3

Physical and mental health

Body mass index	Underweight (BMI < 18.5 kg/m ²)	3.5
	Normal weight (BMI ≥ 18.5 to < 25.0 kg/m ²)	55.8
	Overweight (BMI ≥ 25 to < 30.0 kg/m ²)	30.6
	Obesity (BMI ≥ 30 kg/m ²)	10.0
Hypertension	No	73.9
	Yes	26.1
High cholesterol	No	82.8
	Yes	17.2
Diabetes	No	95.7
	Yes	4.3
Chronic disease ³	No	68.8
	Yes	31.2
Visit to a physician within the past year	No	21.7
	Yes	78.3
Self-perceived health	Good, very good	84.1
	Fair, poor, very poor	15.9
Psychological distress ⁴	Low	82.1
	Moderate, high	17.9
Depression ⁵	No	95.4
	Yes	4.6
Loneliness	Never	64.1
	Sometimes	31.7
	Quite often	2.7
	Very often	1.5

¹ Weighted according to the Swiss general population

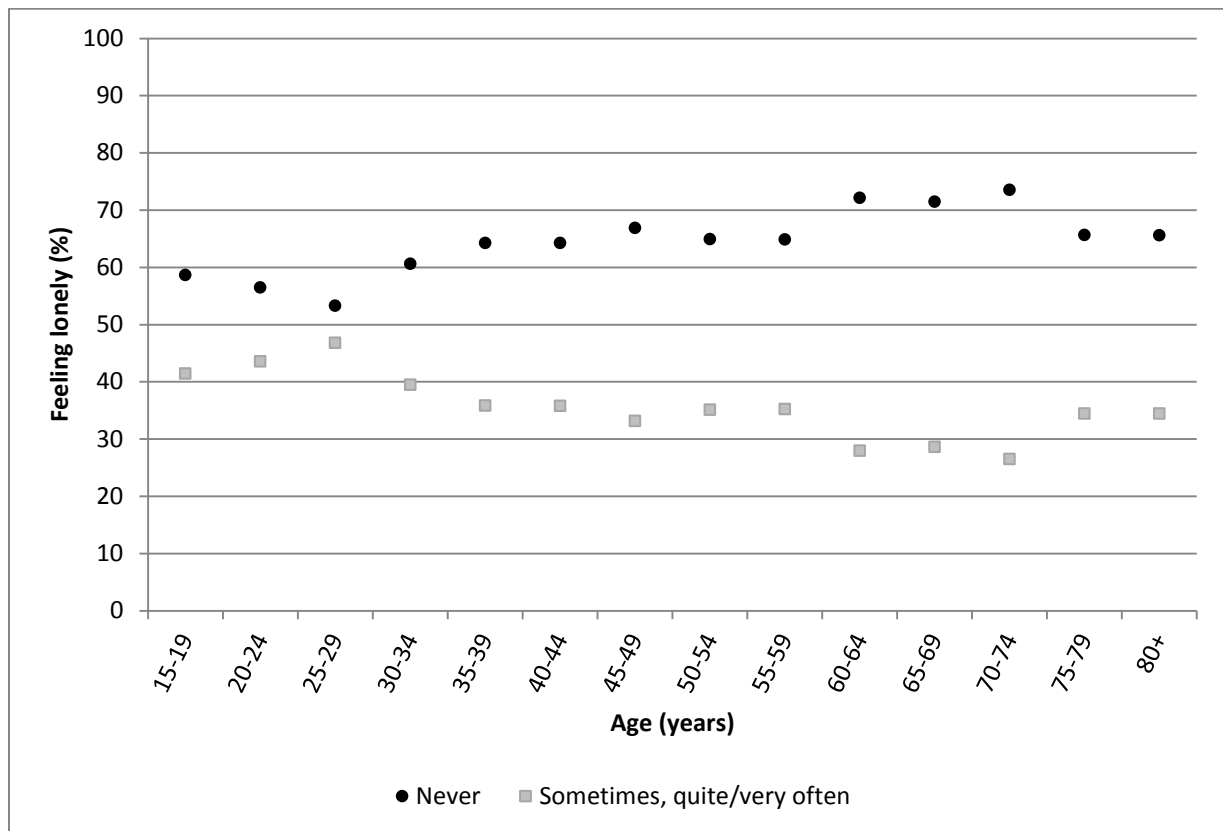
² Ethanol ≥ 20 g/day for women, ≥ 40 g/day for men

³ Ongoing disease or health problem lasting for at least 6 months or expected to last further than 6 months

⁴ Measured by the 5-item mental health index

⁵ Depression: measured by the PHQ-9 from the written questionnaire

Fig. 1 Prevalence of perceived frequency of loneliness by 5-years age groups



CHAPTER 3

Tab. 2: Associations between loneliness and lifestyle and health-related factors of the 2012 Swiss Health Survey¹

		unadjusted		age and sex adjusted		multivariable adjusted	
		OR	95% CI	OR	95% CI	OR	95% CI
Lifestyle factors							
Smoking status	Never and ever smokers	1		1		1	
	Current smokers	1.06	[0.99,1.14]	1.18	[1.09,1.27]	1.13	[1.05,1.23]
Chronic alcohol consumption ²	No	1		1		1	
	Yes	0.99	[0.84,1.16]	1.04	[0.88,1.23]	1.03	[0.87,1.22]
Binge drinking	No	1		1		1	
	Yes	1.01	[0.93,1.09]	1.05	[0.96,1.15]	1.09	[0.99,1.19]
Physical activity	≥ 150 min. per week	1		1		1	
	< 150 min. per week	1.30	[1.20,1.41]	1.31	[1.21,1.43]	1.20	[1.10,1.31]
Pay attention to diet	Yes	1		1		1	
	No	0.97	[0.89,1.05]	0.99	[0.91,1.08]	0.97	[0.89,1.06]
Adherence to the 5-a-day recommendation	Yes	1		1		1	
	No	1.13	[1.00,1.27]	1.32	[1.17,1.49]	1.21	[1.07,1.37]
Physical and mental health							
Body mass index	BMI < 25.0 kg/m ²	1		1		1	
	BMI ≥ 25.0 kg/m ²	0.76	[0.70,0.82]	0.94	[0.87,1.02]	0.93	[0.86,1.01]
Hypertension	No	1		1		1	
	Yes	0.89	[0.82,0.97]	1.09	[1.00,1.20]	1.07	[0.97,1.17]
High cholesterol	No	1		1		1	
	Yes	1.04	[0.95,1.14]	1.33	[1.20,1.47]	1.31	[1.18,1.45]
Diabetes	No	1		1		1	
	Yes	1.06	[0.89,1.25]	1.40	[1.18,1.67]	1.40	[1.16,1.67]
Chronic disease ³	No	1		1		1	
	Yes	1.26	[1.17,1.37]	1.42	[1.31,1.54]	1.41	[1.30,1.54]
Visit to a physician within the past year	No	1		1		1	
	Yes	1.34	[1.22,1.47]	1.26	[1.15,1.39]	1.29	[1.17,1.42]
Self-perceived health	Good, very good	1		1		1	
	Fair, poor, very poor	1.81	[1.65,1.99]	2.13	[1.92,2.36]	1.94	[1.74,2.16]
Psychological distress ⁴	Low	1		1		1	
	Moderate, high	4.12	[3.74,4.55]	4.05	[3.66,4.47]	3.74	[3.37,4.16]
Depression ⁵	No	1		1		1	
	Yes	3.43	[2.75,4.28]	3.09	[2.47,3.87]	2.78	[2.22,3.48]

¹ Weighted according to the Swiss general population and adjusted for age, sex, area of residence, nationality, educational level, marital status, household size and social support

² Ethanol ≥ 20 g/day for women, ≥ 40 g/day for men

³ Ongoing disease or health problem lasting for at least 6 months or expected to last further than 6 months

⁴ Measured by the 5-item mental health index

⁵ Measured by the PHQ-9 from the written questionnaire

CHAPTER 3

Tab. 3: Multivariable adjusted associations between loneliness and lifestyle and health-related factors stratified by age group of the 2012 Swiss Health Survey¹

<i>Loneliness</i>	<i>BMI²</i>			<i>Smoking³</i>			<i>Visit to a physician within the past year⁴</i>			<i>Self-perceived health⁵</i>		
	<i>Ref.</i>	<i>OR</i>	<i>95% CI</i>	<i>Ref.</i>	<i>OR</i>	<i>95% CI</i>	<i>Ref.</i>	<i>OR</i>	<i>95% CI</i>	<i>Ref.</i>	<i>OR</i>	<i>95% CI</i>
Age groups (years)												
≥15 to <30	1	0.83	[0.67,1.03]	1	1.21	[1.02,1.44]	1	1.00	[0.82,1.23]	1	1.98	[1.37,2.85]
≥30 to <60	1	0.92	[0.82,1.03]	1	1.11	[1.00,1.24]	1	1.32	[1.16,1.51]	1	2.19	[1.88,2.54]
≥ 60	1	1.00	[0.86,1.16]	1	1.06	[0.91,1.24]	1	1.80	[1.40,2.31]	1	1.64	[1.40,1.94]
<i>P-Interaction⁶</i>			<i>0.026</i>			<i>0.004</i>			<i>0.004</i>			<i>0.044</i>

¹ Weighted according to the Swiss general population and adjusted for sex, area of residence, nationality, educational level, marital status, household size and social support

² Body mass index < 25.0 kg/m² vs. ≥ 25.0 kg/m²

³ Never smokers vs. ever and current smokers

⁴ No vs. Yes

⁵ Good, very good vs. fair, poor, very poor

⁶ Interactions by age groups and loneliness for health outcomes assessed by Wald tests

Chapter 3

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CHAPTER 4

Lifestyle and health-related predictors of cervical cancer screening attendance in a Swiss population-based study

Aline Richard^{1*}, Sabine Rohrmann¹, Seraina M. Schmid^{2,3}, Brigitte Frey Tirri⁴, Dorothy J. Huang⁵, Uwe G  th^{6,7}, Monika Eichholzer¹

¹ University of Zurich; Epidemiology, Biostatistics and Prevention Institute,
Division of Chronic Disease Epidemiology, Hirschengraben 84, CH-8001 Zurich, Switzerland

² Spital Grabs, Department of Gynecology & Obstetrics
Spitalstrasse 44, CH-9472 Grabs, Switzerland

³ Breast Center St. Gallen, Rorschacher Strasse 150, CH-9006 St.Gallen, Switzerland

⁴ Cantonal Hospital Baselland, Department of Gynecology & Obstetrics,
Rheinstrasse 26, CH-4410 Liestal, Switzerland

⁵ University Hospital Basel, Department of Gynecology and Obstetrics;
Spitalstrasse 21, CH-4031 Basel, Switzerland

⁶ Cantonal Hospital Winterthur, Department of Gynecology and Obstetrics,
Brauerstrasse 15, CH-8401 Winterthur, Switzerland

⁷ Breast Center "Senosuisse", Brauerstrasse 15, CH-8401 Winterthur, Switzerland

* Corresponding author

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Abstract

Background: Since the implementation of cervical cancer (CC) screening, incidence and mortality rates have decreased worldwide. Little is known about lifestyle and health-related predictors of cervical cancer screening attendance in Switzerland. Our aim was to examine the relationship between lifestyle and health-related factors and the attendance to CC screening in Switzerland.

Methods: We analyzed data of 20-69 years old women (n=7,319) of the Swiss Health Survey (SHS) 2012. Lifestyle factors included body mass index, smoking status, alcohol consumption, physical activity and attention to diet. Health-related factors of interest were diabetes, hypertension, high cholesterol levels, chronic diseases, self-perceived health, and psychological distress.

We performed multivariable logistic regression analyses with the dichotomized CC screening status as outcome measure and adjusted for demographic factors.

Results: Obesity, low physical activity, and not paying attention to diet were statistically significantly associated with lower CC screening participation. High cholesterol levels and history of chronic diseases were statistically significantly positively associated with screening participation.

Conclusion: Being obese, physically inactive and non-attention to diet are risk factors for CC screening attendance. These findings are of importance for improving the CC screening practices of low-user groups.

Keywords: Cervical cancer, screening, lifestyle, health, Switzerland

Introduction

Cervical cancer (CC) is the second most common cancer in women worldwide, although incidence and mortality have decreased markedly (National Institute for Cancer Epidemiology and Registration, 2011, Ferlay et al., 2013), following the introduction of the Papanicolaou (PAP) test for cervical cancer. It is estimated that CC screening reduces cervical cancer incidence by approximately 80% (IARC, 2005, Arbyn et al., 2009). In Switzerland, which provides a broad, opportunistic screening system, CC screening has been promoted since the late 1960s. This resulted in a reduced CC incidence, from 440 new cases in 1980 to 210 cases in 2007 (National Institute for Cancer Epidemiology and Registration, 2011). Recommendations of the Swiss Federal law of health insurance for CC screening in Switzerland include one Pap smear every three years after two annual negative results from the age of 18 until 69 years (Arbeitsgruppe "Guideline, 2005). In general, women are invited by their gynecologist for the examination. The CC screening time interval depends on the doctor's personal judgment. For CC screening there is no organized program in Switzerland.

So far, it has been shown convincingly that demographic factors are of importance in relation to CC screening attendance. Accordingly, a systematic review found a positive association of educational level and financial status with CC screening attendance (Limmer et al., 2014). Furthermore, being married was associated with higher attendance in different ethnicities. In contrast, age appears to be inversely associated to CC screening. Another review observed a lower participation rate in screening in older, uninsured, homeless and migrant women with language barriers, in women who have sex with women, and in obese women (Brankovic et al., 2013). According to the 2007 Swiss Health Survey, women with Swiss nationality and high educational level adhered more often to CC screening than non-Swiss women and women with only compulsory education (Oncosuisse, 2011).

Only few studies examined the associations of lifestyle and health factors with CC screening attendance. Nelson et al. reported that smokers, obese women and women with psychological distress participated less often in CC screening (Nelson et al., 2009). Obesity was shown to be a predictor of lower CC screening attendance in a variety of studies; nonetheless, opposite or null results between obesity and screening participation were observed in some other studies (Aldrich and Hackley, 2010, Cohen et al., 2008). A systematic review came to the conclusion that perceived screening facilities-related barriers and

perceived psychological barriers to CC screening were associated with lower screening participation (Bukowska-Durawa and Luszczynska, 2014).

Chronic diseases, such as diabetes or hypertension were negatively associated with CC screening attendance (Kiefe et al., 1998, Liu et al., 2014, Tabaei et al., 2005) in some but not all studies (Lopez-de-Andres et al., 2010). Regarding associations between mental health and CC screening attendance, a lower screening participation among women with mental health problems such as depression or psychological distress was observed (Ludman et al., 2010, Xiang, 2015).

To our knowledge, there is no information about associations of lifestyle factors and health-related factors with CC screening attendance in Switzerland. Thus, we assessed lifestyle factors (body mass index [BMI], smoking status, alcohol consumption, physical activity, attention to diet and health-related factors (diabetes, hypertension, cholesterol, self-perceived health, psychological distress, and chronic disease) that may affect CC screening participation.

Methods

Study population and design

We used data of the cross-sectional 2012 Swiss Health Survey (SHS), which is conducted every five years since 1992 by the Swiss Federal Office of Statistics (SFSO) (Legal basis: Ordinance of the Conduct of Federal Statistical Surveys of 30 June 1993). This population-based survey provides information on health status, several lifestyle and demographic factors and the utilization of health services. A total number of 41,008 participants were randomly selected by a sampling technique based on registries of inhabitants including Swiss and foreigners with a work permit aged 15 years and older and living in a private household. A computer-assisted telephone interview (CATI) was performed and German-, French-, or Italian-speaking individuals were included. The participation rate was 54% amounting to 21,597 individuals. Weighting factors were then used to improve the level of representation of the sample for the Swiss population.

A total of 11,314 women participated in the SHS 2012. After including only women aged 20-69 years (n=8,816) with available information on CC screening participation, our sample

consisted of 7,556 women. After excluding women with missing information on demographic factors (n=28), lifestyle factors (n=96) and diseases (n=113), our final sample consisted of 7,319 women.

Measurements

Variables of interest: As lifestyle factors we included BMI categorized into underweight (BMI <18.5 kg/m²), normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25.0-29.9 kg/m²) and obesity (BMI ≥ 30 kg/m²) (National Institutes of Health, 1998), smoking status (never, former, current), chronic alcohol consumption associated with health risk (≥20 gram ethanol daily vs. less) (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2010), physical activity (≥ 150 minutes per week moderate physical activity and/or one sweating episode per week vs. less) (Bundesamt für Sport BASPO et al., 2013), and paying attention to diet (yes vs. no). As health-related factors we included self-reported chronic conditions such as diabetes, hypertension, high cholesterol levels (assessed by the question: “Have you ever been told by a medical doctor that you were affected by...”) and chronic diseases (ongoing diseases or health problems lasting for at least six months or expected to last a further six months). In addition, self-perceived health status (fair, poor, very poor vs. very good, good) was examined. For the assessment of psychological distress (low, moderate, high) during the previous four weeks, the 5-item mental health index [MHI-5] was used (Berwick et al., 1991).

Outcome Variable: CC screening status was calculated based on the date of the interview and the self-reported information of the date of the last CC screening and then dichotomized in ≤3 years since most recent screening vs. >3 years or never.

Covariates: Demographic variables were used as adjustment factors based on the known associations regarding CC screening participation. Demographics included age, region of Switzerland (German vs. French vs. Italian), area of residence (urban vs. rural), nationality (Swiss vs. non-Swiss), educational level (low [compulsory education or less] vs. middle [secondary education] vs. high [tertiary education]), and marital status (married, registered partnership vs. single, divorced, dissolved, separated, widowed).

Statistical analyses

All statistical analyses were conducted using STATA software version 13.1 (College Station, Texas). Descriptive statistics were computed in percentages for socio-demographic, lifestyle

and health-related factors. We conducted logistic regression analyses to determine the association of each single lifestyle and health-related factor with CC screening participation. We provided unadjusted results and results adjusted for demographic factors (age, region of Switzerland, area of residence, nationality, educational level, and marital status as odds ratios (OR) with the corresponding 95% confidence intervals (95% CI). Furthermore, to account for a possible non-response bias, we performed a sensitivity analysis with the women aged 20-69 years, who were not included in the analyses because of missing or unclear information on screening status.

Sampling weights of the telephone interviews were provided by the SFSO and applied to the data of the present analyses to calculate descriptive characteristics (percentages) and to conduct logistic regression analyses. The sampling weights include a comparison with the permanent 2012 Swiss population with regard to sex, age, geographic region and nationality (Swiss vs. others).

Results

Table 1 shows the distribution of demographic, lifestyle, and health-related factors of the study sample (n=7,319). Participation rate for CC screening within the last three years was 72.9% compared to 9.3% of the women who had participated more than 3 years ago, and 17.8% of the women who had never attended screening.

More than two-thirds of the women lived in the German-speaking region, less than one third lived in the French-speaking region, and the remaining 5.1% in the Italian-speaking region. Overall, living in urban areas was reported by 73.1%. Most of the participants were Swiss and had a middle educational level. Living in a partnership (married or registered partnership) was more frequently reported than being single, divorced/dissolved, separated or widowed (54.3% vs. 45.7%, respectively).

At least half of the included women reported a normal BMI (18.5–24.9 kg/m²), no history of smoking, low chronic alcohol consumption, regular physical activity, and paid attention to their diet.

Diabetes was observed in 2.6% of women, hypertension in 18.8%, and high cholesterol levels in 12.9%. More than two-thirds of the women reported a history of chronic diseases, but the

majority considered their self-perceived health as good and their psychological distress as low.

A sensitivity analysis revealed that the mean age of women excluded from our analyses differed with respect to the mean age compared to our sample (45.3 vs. 40.9 year). In contrast, more included women were of Swiss nationality (77.5% vs. 69.2%), had a high (27.2% vs. 22.5%) or middle (61.2% vs. 53.5%) educational level, and were more often not in a partnership (45.7% vs. 37.1%) compared to the non-included women.

Table 2 shows the association of lifestyle and health-related factors with CC screening participation within the previous three years versus more than three years or never. Overweight and obese women had statistically significantly lower odds of attendance in CC screening than normal weight women in the unadjusted model. After adjustment for demographic factors, the results were attenuated for overweight but remained statistically significant for obese women (OR 0.64, 95% CI 0.51-0.81). Ex-smokers adhered to CC screening statistically significantly more often than women who had never smoked (reference) (OR 1.37, 95% CI 1.14-1.65; multivariable adjustment). Women who were physically active for less than 150 minutes per week had statistically significantly lower odds for CC screening participation compared to the more physically active women (OR 0.85, 95% CI 0.74-0.99; multivariable adjustment). We observed a statistically significantly lower odd of CC screening attendance (OR 0.82, 95% CI 0.69-0.96, multivariable adjustment) in women who reported not paying close attention to their diet.

Neither diabetes nor hypertension was associated with CC screening attendance. Women with high cholesterol levels were more likely to participate in CC screening than women with normal cholesterol levels. The OR was statistically significant in the multivariable model (OR 1.45, 95% CI 1.19-1.77). Regarding health-related factors, chronic diseases were statistically significantly associated with higher odds of CC screening attendance in the unadjusted and multivariable adjusted model (OR 1.19, 95% CI 1.03-1.37 and OR 1.28, 95% CI 1.11-1.48, respectively). Self-perceived health and psychological distress were not associated with CC screening participation.

Discussion

In the present study, among lifestyle factors, individuals participated significantly less in CC screening if they reported being obese, not having regular physical activity, or not paying attention to diet. Prior smoking, on the other hand, was associated with higher attendance than non-smoking. Concerning health-related factors, having high cholesterol levels and/or chronic diseases were positively associated with screening participation. All results were adjusted for various socio-demographic factors.

The participation rate in CC screening of the 20-69 year-old women living in Switzerland within the last three years (72.9%) lies within the range of other European countries. Participation rates vary depending on type of screening program (opportunistic or organized) and local CC screening recommendations. Participation rates amounted to 61% in Belgium (Arbyn et al., 2014), 86.6% in Norway (Hansen et al., 2011), between 78.5% and 83.5% in England (Bang et al., 2012), and 70% in Austria (Breitenecker, 2009).

A persistent human papillomavirus (HPV) infection is necessary but may not be sufficient alone for the development of cervical cancer. Thus, whether a woman will develop cervical cancer seems to depend on a number of additional factors (Burd, 2003). Accordingly, several, but not all studies have shown that obesity is associated with increased risk for cervical cancer, particularly adenocarcinoma (Webb, 2013, Lacey et al., 2003, Tornberg and Carstensen, 1994). There is also limited evidence that obesity is associated with cervical cancer mortality (Calle et al., 2003, Lee et al., 2013). In this context, it is of importance to note that obese women, as in the present study, may be screened less frequently for CC than women of normal weight (Wee et al., 2000, Ostbye et al., 2005, Bussiere et al., 2014, Fontaine et al., 2001, Maruthur et al., 2009), even though the evidence is not entirely consistent (Kim et al., 2009, Reidpath et al., 2002). As Maruthur et al. (2009) pointed out, there are several potential barriers to CC screening participation for overweight and obese women. Apart from equipment-related impediments, the fear of discomfort and pain from the medical examination, being embarrassed or afraid of undergoing testing, unwanted criticisms due to excess weight, uninvited advice to reduce body weight, and lack of respect from medical doctors may play a role (Bussiere et al., 2014, Maruthur et al., 2009).

As in the present study, several other surveys found unhealthy behaviors such as low levels of physical activity (Ostbye et al., 2005, Muus et al., 2012, Coughlin et al., 2004, Abdullah and

Leung, 2001), cigarette smoking (Vander Weg et al., 2012, Byrne et al., 2010), hazardous alcohol consumption (Sicsic and Franc, 2014) and low fruit and vegetable consumption/unbalanced diet (Abdullah and Leung, 2001) to be associated with lower rates of CC screening participation. It should be noted that only one (Coughlin et al., 1999) of these studies adjusted for body weight. Women with unhealthy behaviors may be less health conscious than individuals with healthy habits, and thus, less likely to adhere to regular cancer screening (Muus et al., 2012). Accordingly, Galan et al. (2006) observed in their cross-sectional study in Spain that the clustering of behavioral risk factors (tobacco smoking, hazardous alcohol consumption, leisure-time sedentariness and unbalanced dietary habits) was associated with greater non-attendance to the recommended CC screening. Similarly, in a cross-sectional analysis of the US 2000 National Health Interview data, a healthier lifestyle including non-smoking, physical activity, high fruit and vegetable and low alcohol consumption was significantly positively associated with CC screening use (Meissner et al., 2009). However, the association between smoking and CC screening attendance seems to be multifaceted. Vander Weg et al. observed in their cross-sectional analysis of data from the U.S. 2008 Behavioral Risk Factor Surveillance System that former smokers had a higher compliance with CC screening attendance than daily smokers and women who had never smoked (Vander Weg et al., 2012). The authors hypothesized that former smokers who are more health conscious may be more likely to both stop smoking and to participate in CC screening. We observed similar results in the present study and hypothesize that the higher compliance of former smokers with CC screening might also be the consequence of an increased risk of smokers for cervical dysplasia with the corresponding necessity for regular screening.

Another determinant of CC screening attendance may be an individual's health status (Schumacher et al., 2008). In the present study, reported chronic diseases (ongoing disease or health problem lasting for at least six months or expected to last a further six months) were associated with higher odds of CC screening attendance compared to no chronic diseases. Furthermore, in a cross-sectional Spanish study, CC screening attendance was positively associated with osteomuscular disease (Lopez-de-Andres et al., 2010). The authors argued that the presence of medical conditions might increase the opportunity of receiving cancer screening because of more frequent contact with healthcare providers.

Other studies found inverse associations between history of chronic diseases and CC screening attendance (Kiefe et al., 1998, Liu et al., 2014, Tabaei et al., 2005). Additionally, a recent visit to a primary care provider or having had a recent routine check-up was a predictor of CC screening in some studies (Nascimento et al., 1996, de Quadros et al., 2004, Martins et al., 2009).

High blood cholesterol levels were positively associated with CC screening participation. We hypothesize that high cholesterol levels represents a poor health status, which is normally associated with a visit to a physician. On the other hand, it might also reflect the fact that those women, who had had other screening tests (e.g. BC screening, cholesterol check), are more likely to attend CC screening in addition (Carruth et al., 2006, Borrayo et al., 2004, Martins et al., 2009).

Mental health, on the other hand, was not related to CC screening participation in the present study. Previous surveys examining this association have found varying results (Xiang, 2015). Accordingly, a systematic review by Aggarwal et al.(2013) included 15 studies that examined breast and CC screening attendance among women with mental diseases such as depression, anxiety, schizophrenia and psychosis. In seven of these studies, mental illness was associated with lower cancer screening attendance.

Some of the discussed factors may also impair attendance to screening other than CC screening (Lagerlund et al., 2015, Gimeno Garcia, 2012). Obese individuals, for example, might be less likely than non-obese persons to be screened for colorectal and breast cancer (Ferrante et al., 2006, Eichholzer et al., 2015) even though the evidence is not consistent.

The current study has several positive features including the large, nationally representative sample of individuals 20-69 years living in Switzerland and the comprehensiveness of its data allowing for adjustment for a number of important covariates associated with lifestyle/health-related factors and CC screening attendance. Nevertheless, it is a cross-sectional survey, thus causal and directional conclusions are precluded. The fact that receipt of CC screening and studied lifestyle and health factors were based solely on self-report and were not physician-confirmed is another limitation. Self-reported screening behaviors from national surveys often overestimate screening use (Howard et al., 2009). In addition, body height and weight, were also not clinically assessed. Previous studies have shown that weight is often under-reported, especially in overweight females, leading to an

underestimation of BMI (Faeh et al., 2008). Moreover, due to the low overall response rate of 54% in the SHS, the possibility of response bias cannot be ruled out. The use of weighting factors, nevertheless, allows for the extrapolation of the results in relation to age, sex, region and nationality from the sample to the total population living in Switzerland (SFSO). In addition, even though we controlled for educational level as a proxy for socio-economic factors that may be associated with both CC screening participation and lifestyle and health factors, residual confounding cannot be excluded, such as that financial status is known to affects the CC participation rate.

Furthermore, women with valid information on CC screening status differed in respect to demographic factors from the non-included women, which had missing or unclear information on CC screening participation. Thus, although we controlled for demographic factors, there may be a response bias, such as that screening status was more often reported in women with high educational level. Finally, factors that may be significant determinants of CC screening attendance such as knowledge and beliefs about the benefits of CC screening, were not recorded in the current study (Klug et al., 2005, Lo et al., 2013).

In conclusion, being overweight or obese, physically inactive and not paying attention to diet are risk factors for non-attendance to CC screening. Being affected by chronic diseases and high cholesterol levels on the other hand, were associated with higher odds of CC screening attendance in Switzerland. These findings are of importance for improving the CC screening practices of the low user groups in Switzerland.

Conflict of Interest statement

The authors declare that there are no conflicts of interest.

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Chapter 4

Tables and Figures

Tab. 1: Baseline characteristics (demographic, lifestyle and health related factors) of 18-69 years old women of the 2012 Swiss Health Survey¹

		Total
Women, n		7319
Age, mean		43.9
		%
Cervical cancer screening	Never	17.8
	Within the last 3 years	72.9
	More than 3 years ago	9.3
Demographic factors		
Age (years)	≥ 20 to < 30	19.5
	≥ 30 to < 40	20.3
	≥ 40 to < 50	25.7
	≥ 50 to < 60	18.9
	≥ 60 to < 70	15.5
Region of Switzerland	German region	68.7
	French region	26.2
	Italian region	5.1
Area of residence	Urban	73.1
	Rural	26.9
Nationality	Swiss	77.5
	Non-Swiss	22.5
Educational level	High	27.2
	Middle	61.2
	Low	11.6
Marital status	married / registered partnership	54.3
	Single, divorced / dissolved partnership, separated, widowed	45.7
Lifestyle factors		
BMI	Underweight (BMI < 18.5 kg/m ²)	5.9
	Normal weight (BMI ≥ 18.5 to < 25.0 kg/m ²)	65.0
	Overweight (BMI ≥ 25 to < 30.0 kg/m ²)	20.8
	Obesity (BMI ≥ 30 kg/m ²)	8.3
Smoking status	Never smokers	52.5
	Ex-smoker	20.2
	Current smokers	27.3
Alcohol ≥ 20 g/day	No	96.2
	Yes	3.8
Physical activity	≥ 150 min. per week	71.0
	< 150 min. per week	29.0
Attention to diet	Yes	76.3
	No	23.7
Health-related factors		
Diabetes	No	97.4
	Yes	2.6

CHAPTER 4

Hypertension	No	81.2
	Yes	18.8
High cholesterol	No	87.1
	Yes	12.9
Chronic diseases ²	No	69.1
	Yes	30.9
Self-perceived health	Good, very good	85.3
	Fair, poor, very poor	14.7
Psychological distress	Low	78.6
	Moderate	15.1
	High	6.3

¹ all proportions are weighted, except n

² ongoing diseases or health problem lasting for at least 6 months or expected to last further 6 months

Tab. 2: Associations of lifestyle and health related factors with participation in cervical cancer screening¹ in women 20-69 years; Swiss Health Survey from 2012

		unadjusted		adjusted for demographic factors ²	
		OR	95% CI	OR	95% CI
Lifestyle factors					
BMI	Normal weight (BMI ≥ 18.5 to < 25.0 kg/m ²)	1		1	
	Underweight (BMI < 18.5 kg/m ²)	0.92	[0.68,1.24]	0.95	[0.70,1.30]
	Overweight (BMI ≥ 25 to < 30.0 kg/m ²)	0.81	[0.69,0.95]	0.89	[0.75,1.05]
	Obesity (BMI ≥ 30 kg/m ²)	0.57	[0.46,0.72]	0.64	[0.51,0.81]
Smoking status	Never smokers	1		1	
	Ex-smoker	1.33	[1.11,1.59]	1.37	[1.14,1.65]
	Current smokers	0.95	[0.82,1.11]	1.07	[0.91,1.25]
Alcohol ≥ 20 g/day	No	1		1	
	Yes	0.99	[0.73,1.34]	1.07	[0.78,1.47]
Physical activity	≥ 150 min. per week	1		1	
	< 150 min. per week	0.79	[0.69,0.91]	0.85	[0.74,0.99]
Attention to diet	Yes	1		1	
	No	0.69	[0.59,0.80]	0.82	[0.69,0.96]
Health-related factors					
Diabetes	No	1		1	
	Yes	0.79	[0.57,1.11]	1.00	[0.70,1.43]
Hypertension	No	1		1	
	Yes	0.85	[0.73,1.00]	0.97	[0.82,1.15]
High cholesterolin	No	1		1	
	Yes	1.19	[0.99,1.43]	1.45	[1.19,1.77]
Chronic diseases ³	No	1		1	
	Yes	1.19	[1.03,1.37]	1.28	[1.11,1.48]
Self-perceived health	Good, very good	1		1	
	Fair, poor, very poor	0.84	[0.70,1.00]	1.06	[0.88,1.28]
Psychological distress ⁴	Low	1		1	
	Moderate	0.92	[0.77,1.10]	1.00	[0.83,1.20]
	High	0.78	[0.59,1.03]	0.91	[0.67,1.24]

¹ CC screening adherence defined by participation within last 3 years and weighted according the Swiss general population

² adjusted for age, region of Switzerland, area of residence, nationality, educational level, marital status

³ ongoing diseases or health problem lasting for at least 6 months or expected to last further 6 months

⁴ measured by the 5-item mental health index

Chapter 4

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CHAPTER 4

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CHAPTER 5

Prevalence of vitamin D deficiency and its associations with skin color in pregnant women in the first trimester in a sample from Switzerland

Aline Richard¹, Sabine Rohrmann¹, Katharina C. Quack Lötscher^{2*}

Short title: Skin color and Vitamin D in pregnant women

¹ University of Zurich; Epidemiology, Biostatistics and Prevention Institute,

Division of Chronic Disease Epidemiology; Hirschengraben 84, CH-8001 Zurich, Switzerland

² University Hospital Zurich; Clinic of Obstetrics, Frauenklinikstrasse 10, 8091 Zurich, Switzerland

* Corresponding author

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Abstract

Objectives: Vitamin D deficiency in pregnancy has negative clinical consequences, such as associations with glucose tolerance, and has been shown to be distributed differently in certain ethnic groups. We examined the prevalence of vitamin D deficiency (< 20 ng/mL) in women in early pregnancy in Switzerland and evaluated the association of skin color with vitamin D deficiency.

Study design: In a single-center cohort study validated Fitzpatrick scale and objective melanin index were used to determine skin color. Vitamin D was measured by electrochemiluminescence immunoassay.

Results: In the study 204 pregnant women were included. Almost two third of all women were vitamin D deficient. Mean serum vitamin D concentration was 26.10 ng/mL in vitamin D sufficient women and 10.54 ng/mL in women with deficiency. In the most parsimonious model (defined by the Akaike Information Criterion), women with dark skin color were statistically significantly more often vitamin D deficient compared to women with light skin color (OR 2.60; 95% CI 1.08-6.22; adjusted for age, season, vitamin D supplement use, body mass index, smoking, parity).

Conclusion: We observed a high prevalence of vitamin D deficiency among pregnant women and dark skin color was associated with vitamin D deficiency. This calls for more intense counseling to improve vitamin D status during pregnancy, i.e., use of vitamin D supplements during pregnancy, in particular for women with darker skin color.

Keywords: vitamin D, pregnancy, skin color, vitamin D deficiency, Switzerland

Introduction

During the last century, vitamin D fortification programs have largely eradicated health risks of vitamin D deficiency such as rickets and osteomalacia from western populations. However, vitamin D deficiency (< 20 ng/mL) is reemerging and suboptimal vitamin D blood levels are widespread in industrialized nations, specifically in women with darker skin color (1-7). Suboptimal vitamin D level is thought to be associated with a range of diseases such as cardiovascular disease and diabetes (8) as well as with the risk of several types of cancer or depression (9). Cholecalciferol (vitamin D₃) is synthesized in the skin by sunlight (UVB) from 7-dehydrocholesterol, followed by the transformation to the active form 25-hydroxyvitamin D [25(OH)D] in the liver. In a further step, 25(OH)D is metabolized into the physiologically active 1,25-dihydroxyvitamin D [1,25(OH)₂D] in the kidney. As 25(OH)D has a half-life of 15 days, which is longer than for 1,25(OH)₂D, it is considered to be the better indicator of vitamin D status. Individuals living in countries with less sun exposure might be at higher risk for vitamin D deficiency. Additionally, during winter and spring sun exposure is low in northern countries. Besides geographic and weather circumstances, several studies showed that personal characteristics affect vitamin D synthesis. Circulating vitamin D concentrations differ by skin color: Individuals with darker skin produce less vitamin D with the same amount of sunlight exposure than individuals with lighter skin color (10, 11). In Europe, estimated vitamin D levels showed large variation due to risk factors such as immigration status from non-Western countries, low consumption of foods rich in vitamin D or low vitamin D supplementation (12).

In pregnancy, increased calcium and adequate vitamin D levels are required and, thus, pregnant women are in general at higher risk of vitamin D deficiency (6). Vitamin D deficiency in pregnancy has been shown to be associated with a variety of clinical consequences (13-16) that range from negative influence on glucose tolerance, association with preeclampsia to improvement of birth weight by vitamin D supplementation in certain ethnic groups (17).

Currently, vitamin D status of pregnant women living in Switzerland is unknown (18) and hence, the aim of our study was to evaluate vitamin D levels in pregnant women and to determine the prevalence of vitamin D deficiency. Furthermore, we aimed at addressing the question whether the prevalence of vitamin D deficiency differs between women with light or dark skin color, i.e., between specific subgroups of the population living in Switzerland.

Material and Methods

Study population

Between September 2014 and December 2015, 80% of the women visiting the Clinic of Obstetric at the University Hospital Zurich for their first pregnancy visit were recruited for participation in this vitamin D study. The study was approved by the ethics committee of the canton of Zurich, Switzerland (KEK-ZH-Nr. 2013-0213). Exclusion criteria were twin pregnancy, HIV, history of parathyroid, renal or liver disease, chronic malabsorption syndromes or granuloma-forming disorders, age below 18 years or known or suspected drug or alcohol abuse. We collected data of 205 women. Due to 1 missing information on vitamin D status, our final sample consisted of 204 women.

Vitamin D blood samples

After giving informed consent, a blood sample of 10 ml was collected during the routine blood collection of the pregnancy examination. Blood samples were centrifuged and serum was extracted in the Institute of Clinical Chemistry at the University Hospital Zurich within hours after blood sampling. Total 25-hydroxyvitamin D was analyzed on the same day using the vitamin D total-analysis Roche Cobas® electrochemiluminescence immunoassay (Roche Diagnostics, Basel, Switzerland). The method has a detection range of 7.5–175 nmol/l for 25(OH) vitamin D.

Vitamin D deficiency was defined as 25(OH)D concentrations < 20 ng/mL vs. sufficiency as ≥ 20 ng/mL as recommended by the Endocrine Society (19).

Skin color

The physician together with the participant filled out a questionnaire. The skin color of the women was assessed according to the classification by Fitzpatrick (20). This scale allows for differentiating between skin phototypes based on skin reaction to sun exposure. We used an adapted Fitzpatrick scale with five skin types. The classification of skin type was assessed first by showing the participant a picture of the different skin color types (I-V) and second, by asking on what happens to the untanned skin if it is exposed in the early summer at noon for 45 to 60 minutes to the sun. Answers range from “painful sunburn after 24 hours and not tanned after one week” to “Skin is deeply pigmented brown/black, no sunburn and tanned after one week”. Based on the pictures and questions the women estimated their own skin phototype. Additionally, the interviewer evaluated the skin type. When the classification of

pregnant woman and the interviewer disagreed, the rounded arithmetic mean of was used. Skin color type was dichotomized into Fitzpatrick scale I to III vs. IV and V.

Furthermore, the skin type was measured with a DMS II ColorMeter (Cortex Technology, Hadsund, Denmark) resulting in a melanin index (21). The device is a narrow band spectroscopy instrument with a green diode centred on 568 nm and red diode centred on 655 nm. The device was calibrated every week with white balance. Melanin index was measured 3 times on the inner underarm and the arithmetic mean was calculated to categorize melanin in quartiles.

Covariates

Based on the World Bank Map, country of a woman's origin was grouped into five categories; 1) Switzerland and Germany, 2) Northern America and Europe, Central Asia and New Zealand, 3) Southern Europe, Australia, Latin America, 4) South- and East Asia and Pacific, and 5) Africa and Middle East. For further analyses these countries were dichotomized into groups 1 and 2 vs. group 3, 4, and 5. Further covariates were maternal age, week of pregnancy, parity, gravidity, body mass index (BMI), educational level of participant and her partner (less than compulsory education vs. low [compulsory education] vs. middle [secondary education] vs. high [tertiary education]), smoking status (never vs. former vs. current), season of blood collection (winter vs. spring vs. summer vs. fall), number of days per week spent at least 1 hour outdoors in the past half year, sun protection (never vs. sometimes vs. always), fish consumption (only salmon, tuna, mackerels and herring; at least once per week vs. less), vitamin D supplements intake (yes vs. no).

Statistical analyses

All statistical analyses were conducted using STATA software version 13.1 (College Station, Texas). Geometric means were used to illustrate the prevalence of vitamin D deficiency.

Logistic regression analyses were used to determine associations of skin color with vitamin D deficiency. The Akaike Information Criteria (AIC) was used for selecting the final model solution for multivariable adjustment. As a result of the AIC and of dropping variables because of collinearity, we presented the 4 most parsimonious models; 1) adjusted for age, 2) adjusted for age and season, 3) adjusted for age, season, vitamin D supplement intake, BMI and smoking status, and 4) adjusted for age, season, vitamin D supplement intake, BMI, smoking status and. Sensitivity-analyses were performed using the dichotomized countries

of origin and the dichotomized melanin index (by median) instead of the Fitzpatrick scale. Differences between groups were examined using Anova and t-test ($p < 0.05$, two-sided).

Results

Descriptive characteristics of the 204 women are provided in table 1. Almost two third of the women were vitamin D deficient. Mean serum vitamin D concentration was 26.10 ng/mL in vitamin D sufficient women and 10.54 ng/mL in women with deficiency. Light skin color was reported by 88% of the women with sufficient vitamin D levels and from 66.6% with vitamin D deficiency.

Mean age at blood collection was 31.1 and 29.4 years in vitamin D sufficient and deficient women, respectively. About one third of the women with sufficient vitamin D levels and 14% of vitamin D deficient women were of German or Swiss origin. Half of the women with sufficient vitamin D concentration used sometimes sun protection, 13.3% never used it and 36.0% always used sun protection. In women with vitamin D deficiency sun protection was used each “never”, “sometimes” or “always” by one third of women. Fish consumption was reported by 51.4% of the women without and by 45.3% of the women with vitamin D deficiency and vitamin D supplements intake by 8.6% and 8.7% of the women without and with vitamin D deficiency, respectively.

The associations of dark skin color with vitamin D deficiency were assessed with logistic regression using different adjustment models (Table 2). The AIC fitted best for the age-adjusted model with an OR of 3.25 (95% CI 1.46-7.24) for the associations of skin color with vitamin D deficiency. The next model with a good AIC fit included age and season (OR 3.29; 95% CI 1.4-7.36). In the multivariable adjusted model including age, season, vitamin D supplement intake, BMI, smoking status and parity, OR was 2.60 (95% CI 1.08-6.22). In the sensitivity-analysis using dichotomized countries of origin instead of the Fitzpatrick scale, the best AIC fit and the results remained similar (data not shown). However, in the sensitivity-analysis with the dichotomized melanin index as a proxy for skin color the AIC fitted best for the same model as in our main analysis, but the associations of dark skin color with vitamin D deficiency was attenuated and results for models 3 and 4 did not remain statistically significant (data not shown).

According to the results of the AIC, age and season explained the model best. Figure 1 depicts geometric mean vitamin D levels by light and dark skin color type (according to the Fitzpatrick scale) stratified by season. However, differences between seasons were not statistically significant, neither in light-skinned nor in dark-skinned women.

In Figure 2 vitamin D levels were stratified by skin color and vitamin D supplement intake.

Younger women had lower vitamin D levels compared to older women with light and with dark skin color (Fig. 3). Vitamin D levels in women younger than 25 years were 11.8 ng/mL and 8.6 ng/mL in light and dark skin color, respectively. Women aged 35 or above had a mean vitamin D level of 17.6 ng/mL (light skin color) and 14.2 ng/mL (dark skin color). In dark-skin women differences were not statistically significant; in light skin colored women the p-value was 0.06 (Anova).

Comments

In our study, almost two third of the pregnant women were vitamin D deficient and dark skin color was associated with a higher prevalence of vitamin D deficiency.

A recent systematic review looking at vitamin D deficiency in pregnant women in the Mediterranean region observed a prevalence of vitamin D deficiency (defined as ≤ 20 ng/mL) in pregnant women ranging from 22.7% to 90.3% (22). Only 4 out of 15 studies selected included in the systematic review were conducted during the first trimester of pregnancy, with a vitamin D deficiency prevalence ranging from 22.7% to 59% (23-26). Studies conducted in Northern European countries or the US also reported heterogeneous rates of vitamin D deficiency, such as 10% in US in women in early pregnancy or 65% in pregnant women in Sweden (levels < 50 nmol/L, which corresponds to ≤ 20 ng/mL). In Belgium, 47% of pregnant women in the first trimester were vitamin D deficient (27), in the Netherlands 8-62% in 12th week of pregnancy (deficiency defined as < 25 nmol/L) (28), and in Norway 77.4 % of pregnant women in the first trimester had a vitamin D deficiency (29). Thus, our result lies within the range of vitamin D deficiency observed in early pregnancy.

Concerning skin color, our results concur with previous data (28, 30-32) showing that vitamin D deficiency varied by light and dark skin phototype, i.e. dark skin color was significantly associated with vitamin D deficiency. Furthermore, studies consistently show that vitamin D levels among pregnant women in Northern Europe and the US are lower in ethnic minority

groups, which generally have darker skin. Dark-skinned individuals produce less 25(OH)D than individuals with light skin by the same sunlight exposure (UVB) (28, 33-35).

The endogenous skin synthesis through UVB radiation and diet (or vitamin D supplement intake, respectively) are the two main sources of vitamin D. In our study, adjusting for season showed the best model fit, expressed as AIC (including also age as covariate), which serves as a proxy for sunlight. Looking more detailed into vitamin D levels stratified by skin color and seasons women in our study had higher vitamin D levels in summer compared to winter, and vitamin D levels were lower in women with dark than with light skin color, but differences between seasons were not statistically significant. Previous studies described lower vitamin D levels in winter for the general population (33), and for pregnant women most studies found higher vitamin D levels in summer than in winter, but not all tested for statistical significance (6, 36-38).

In our study only a small percentage of women took vitamin D supplements and only half of the women ate fish at least once per week. As vitamin D supplement intake was a good AIC model fit, vitamin D levels stratified by intake and skin color were examined but differences were not statistically significant. A recent meta-analysis and a systematic review observed that supplementing pregnant women with vitamin D leads to higher levels of vitamin D at term (39, 40). We hypothesize that in our study it might be too early in pregnancy to see an effect. From a public health perspective, fortification of food could improve vitamin D levels in all pregnant women. To date, vitamin D fortification of food is more common in the Northern Europe (e.g. Norway, Denmark and Sweden) than in other countries of Europe, such as Switzerland.

We observed that age was an important covariate and that vitamin D levels were higher in older compared to younger pregnant women, although differences were not significant. Results of other studies looking at the relationship between age and vitamin D are contradictory and no association, non-linear association (42) as well as similar results as in our study (43) were observed. A possible explanation for an association with age may be that older individuals are more health conscious than younger pregnant women.

Strengths and limitations

Women included in the study came from a great variety of countries of origin, which allowed having different skin pigmentation colors represented. Switzerland has more than 20% migrant population indicating an urgent need addressing specific needs in this population. A

further strength was the inclusion of a variety of confounders in our study, but due to collinearity, such as from country of origin, melanin index with light and dark skin color according to Fitzpatrick, we could not include these variables in our final multivariable adjusted models. Nevertheless, we performed sensitivity-analyses with these variables, which mostly confirmed our results with the Fitzpatrick scale. A further limitation was that women with dark skin (Fitzpatrick Scale V) were limited in their number and that other factors that affect vitamin D levels were not assessed, such as veiling of the women or physical activity. Also residual confounding cannot be ruled out.

Conclusion

Prevalence of vitamin D deficiency is common in women in early pregnancy. Almost two thirds of all women in our study population had a vitamin D deficiency. We found a difference in 25(OH) vitamin D levels and prevalence depending on maternal skin type emphasizing a consequent screening and supplementation program for mothers with darker skin type.

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Contributor statement: KQL, SR and AR designed the study and planned the analyses. KQL supervised the recruiting of participants. AR performed the analyses and prepared the first draft of the manuscript. All authors contributed to the interpretation of the data and edited the manuscript. SR supervised the study. All authors have approved the final manuscript.

Chapter 5

Tables and Figures

Fig. 1: Vitamin D levels by light and dark skin color and seasons

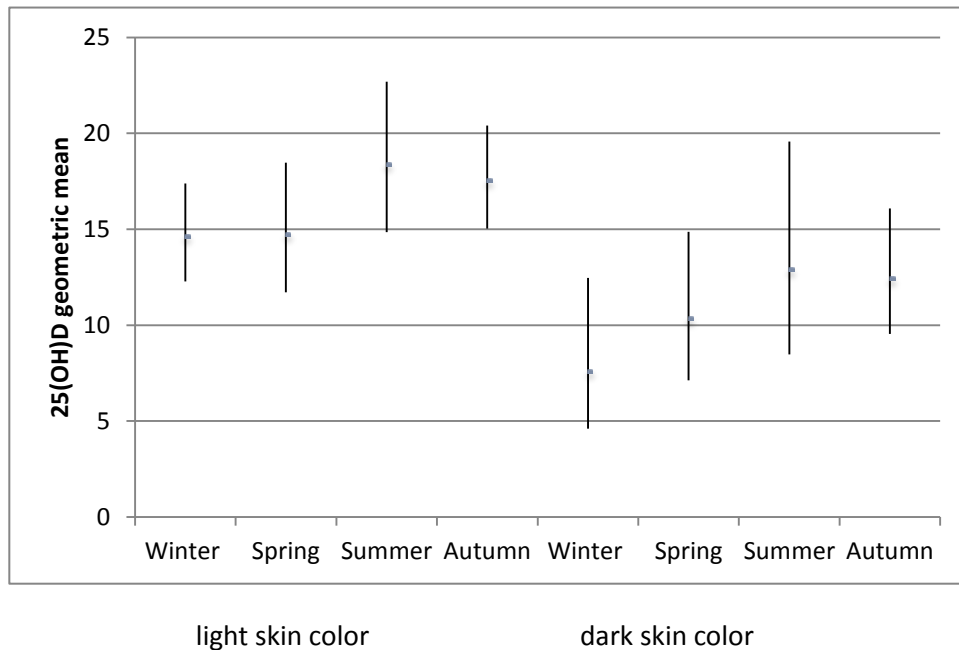


Figure 1 legend: Vitamin D levels stratified by light and dark skin color according to the Fitzpatrick scale (I, II, III vs. IV, V) and seasons (winter= december, january, february; spring= march, april, may; summer=june, july, august; autumn=september, october, november).

Fig. 2: Vitamin D levels by light and dark skin color and vitamin D supplementation status

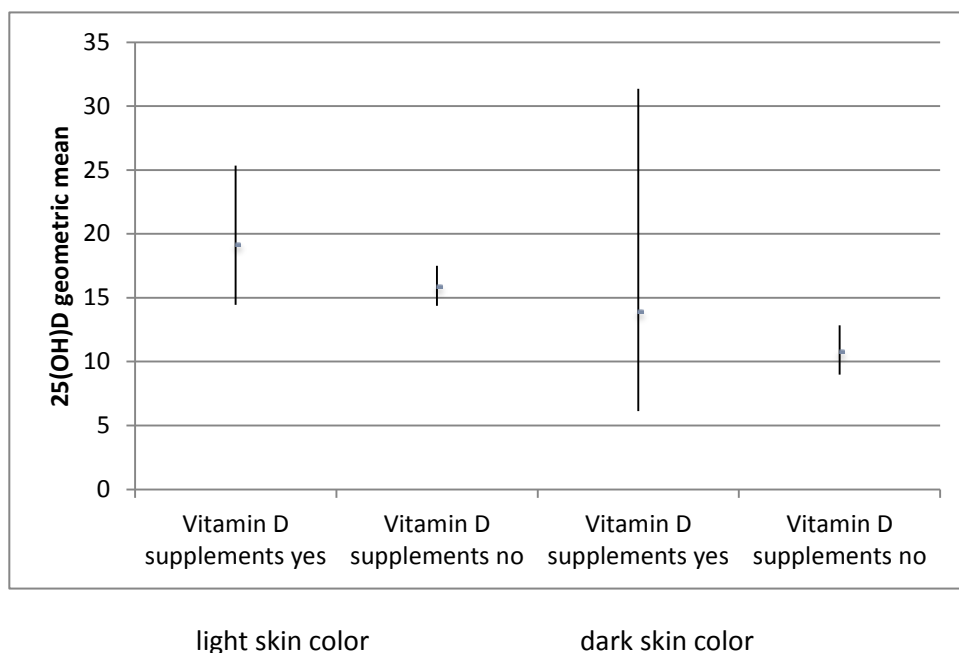


Figure 2 legend: Vitamin D levels stratified by light and dark skin color according to the Fitzpatrick scale (I, II, III vs. IV, V) and vitamin D supplement intake (yes vs. no).

Fig. 3: Vitamin D levels stratified by skin color and age groups

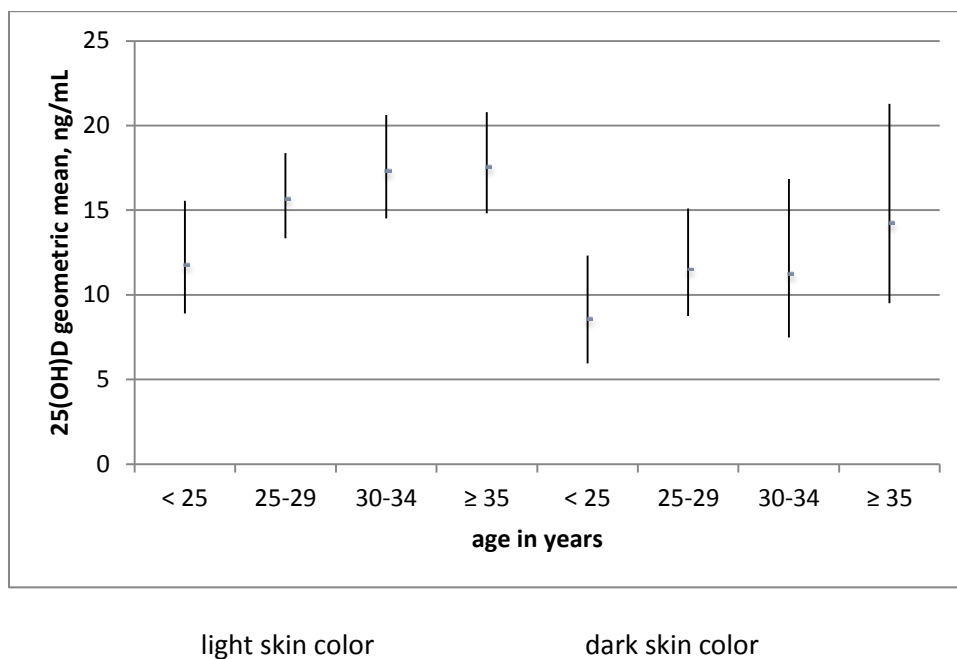


Figure 3 legend: Vitamin D levels stratified by light and dark skin color according to the Fitzpatrick scale (I, II, III vs. IV, V) and four age groups.

CHAPTER 5

Tab. 1: General characteristics of pregnant women with light and dark skin color

	Vitamin D sufficiency ¹	Vitamin D deficiency ²
n (%)	75 (36.8)	129 (63.2)
25(OH)D ng/mL, geometric mean (95% CI)	26.10 (24.76-27.42)	10.54 (9.68-11.48)
Light skin colour ³ , %	88.0	66.6
Melanin levels, median (Q1, Q3)	32.9 (30.8,37.2)	34.3 (30.8,41.8)
Age, mean (SD)	31.1 (4.8)	29.4 (4.8)
Week of pregnancy, median (Q1, Q3)	9 (8,10)	9 (8,10)
Parity, % nulliparous	54.7	51.9
Gravidity, % first pregnancy	42.7	40.3
BMI (kg/m ²) before pregnancy, median (Q1, Q3)	20.7 (19.7,23.1)	22.5 (20.4,25.3)
BMI (kg/m ²) current, median (Q1, Q3)	21.5 (20.1,23.9)	22.8 (20.7,26.2)
Country of origin, %		
Switzerland and Germany	34.7	14.0
North America, Northern Europe, Caucasus, Central asia, New Zealand (without Switzerland and Germany)	28.0	14.9
South Europe and Australia Latin America and the Caribbean	28.0	28.7
South, East Asia and Pacific	5.3	21.7
Africa and middle east	4.0	21.7
Educational level achieved ⁴ , %		
less than compulsory education	2.7	7.8
low education	4.0	15.6
middle education	34.7	32.8
high education	58.7	43.8
Educational level achieved of the partner ⁴ , %		
less than compulsory education	4.0	7.9
low education	2.7	14.3
middle education	33.3	42.9
high education	60.0	34.9
Smoking status, %		
Never smoker	46.7	66.7
Ever smoker	45.3	21.7
Current smoker	8.0	11.6
Season		
Winter	24.0	24.8
Spring	18.7	22.5
Summer	20.0	19.4
Fall	37.3	33.3
Days per week spent at least 1 hour outdoor in the past half year, median (Q1, Q3)	2 (2,5)	3 (2,7)
Using sun protection in summer, %		
Never	13.3	31.3
Sometimes	50.7	31.3
Always	36.0	37.5
Fish consumption at least once per week, %	51.4	45.3
Vitamin D supplements intake, %	8.6	8.7

¹ 25(OH)D ≥ 20 ng/mL

² 25(OH)D < 20 ng/mL

³ Light skin colour defined as values I to III from the Fitzpatrick scale

⁴ Low=compulsory education; middle=secondary education; high=tertiary education

CHAPTER 5

Tab. 2: Associations between skin color and vitamin D deficiency in 204 pregnant women

Dark skin color	No insufficiency (Reference ≥ 20 ng/mL)			
	OR	OR	95 % CI	AIC
age adjusted model	1	3.25	(1.46,7.24)	258.827
age and season adjusted	1	3.29	(1.47,7.36)	264.466
multivariable adjusted model ¹	1	2.56	(1.08,6.11)	265.616
multivariable adjusted model ²	1	2.60	(1.08,6.22)	267.536

¹ Adjusted for age, season, vitamin d supplement intake, BMI, smoking status,

² Adjusted for age, season, vitamin d supplement intake, BMI, smoking status, parity

Chapter 5

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Summary and

Conclusions

Summary and Conclusions

This thesis broadens and contributes to and current knowledge about lifestyle and health in Switzerland by providing data that are representative for the population living in Switzerland. Only chapter 5 is restricted to the Zurich area. In this thesis an emphasis was set on mental health, as epidemiological studies looking at risk factors and outcomes of mental illnesses are still rare compared to epidemiological studies on other NCDs such as cancer and cardiovascular diseases.

In the first chapter, a significant association between adhering to the 5-a-day recommendation for fruit and vegetables and psychological distress was observed for Switzerland. Individuals keeping to the 5-a-day recommendation had a lower likelihood to report moderate or high distress levels than individuals not adhering to this recommendation. To our knowledge, this is the first time associations of this type are reported. Our results are in line with the growing evidence that diet has a beneficial effect on the occurrence and recurrence of mental diseases such as depression. Strengthening efforts to comply with the 5-a-day dietary recommendation might be a successful and cost-effective means to lowering psychological distress.

In chapter two, it was shown that body weight dissatisfaction affected nearly one fourth of the population and was associated with depression. The association was independent of age, sex, and BMI. These results are in accordance with findings from surveys conducted mainly in adolescents looking at the associations of various components of body image with depression (1-6). Thus, our study highlights that associations between body weight dissatisfaction and depression are also seen in the general population. Hence, programs that aim to reduce depression by diminishing body (weight) dissatisfaction should refer to everyone regardless of weight, age and sex.

The analysis in the third chapter showed that loneliness was prevalent in all age groups of adulthood and was associated with unhealthy lifestyle (i.e. smoking, physical inactivity, and non-adherence to the 5-a-day recommendation) and poorer physical and mental health (i.e. report poor self-rated health, visits to medical doctors, hypercholesterolemia, diabetes, chronic diseases, distress, and depression). These results are in line with other studies that observed positive associations between loneliness and health (7-9). For some associations, our analysis provided new results (e.g. with the 5-a-day recommendation). For other associations observed, such as with smoking or hypertension, our null-results were in

Summary and Conclusions

contrast to other studies that found associations between loneliness and these factors. Thus, the results of this analysis contribute to a better awareness of loneliness as an underestimated health risk factor for all ages, and not only among older adults.

In chapter four, being obese, not having regular physical activity, or not paying attention to diet were associated with low cervical cancer screening participation, whereas high cholesterol levels, chronic diseases, and prior smoking were related to higher participation. Only few studies examined the associations of lifestyle and health factors with cervical cancer screening attendance (10-12). Thus, most of the results are contributing to a new knowledge, which are of importance for improving the cervical cancer screening practices of the low-user groups in Switzerland.

In the last chapter, the association of skin color as a biological predisposition with vitamin D deficiency in a sample of pregnant women from the area of Zurich was evaluated. These associations were stronger in women with dark skin color. Our results are in line with a variety of studies (13-16), but to our knowledge this is the first study that assessed prevalence rates of vitamin D deficiency for pregnant women in the Zurich area. As nearly two third of the pregnant women were vitamin D deficient, a consequent screening and supplementation program for expecting mothers, especially with darker skin type should be considered.

In this thesis, some so far unknown associations between lifestyle and health were observed for Switzerland. Several positive features include the large, nationally representative sample of individuals living in Switzerland (chapter 1 to 4). The use of weighting factors allows for the extrapolation of the results with respect to age, sex, region and nationality from the sample to the total population living in Switzerland. A further strength is the comprehensiveness of its data allowing for adjusting for a number of important covariates. However, due to the cross-sectional design, reverse causality cannot be ruled out. But indeed, the importance of the associations between health and lifestyle factors is not necessarily attenuated by the cross-sectional design. In this context, it has to be pointed out that psychological distress (chapter 1), body weight dissatisfaction (chapter 2) and loneliness (chapter 3) are undesired emotional states, but not manifest psychiatric disorders. Thus, from a public health perspective it might be worthwhile to detect these – possibly precursors of mental disorders – and to undertake preventive measures before the

Summary and Conclusions

manifestation of psychiatric disorders, according to the WHO definition of health as the state of complete physical, mental and social well-being. As a further limitation of the SHS 2012, the low overall response rate of 54% in the SHS 2012 has to be mentioned, which possibly leads to a response bias, i.e. a “healthy participant effect”(17).

The strengths and limitation of the vitamin D study (chapter 5) differed due to the different assessment. One strength was that this study included pregnant women visiting the Clinic of Obstetric at the University Hospital Zurich for their first routine pregnancy visit, which allowed for recruiting women of various countries of origin. This resulted in the sampling of different skin color and reflects the migrant population of about 20% in Switzerland. A further strength was the inclusion of a variety of confounders in our study, although some factors that affect vitamin D levels were not assessed (e.g. veiling). A limitation was that the number of women with very dark skin (Fitzpatrick Scale V) was limited.

In conclusion, in this thesis various health and lifestyle associations were newly discovered and, thus, contribute to the awareness of the importance of considering different aspects of lifestyle and health as a basis for future research – e.g. longitudinal cohort studies – or for possible implications towards health and healthy lifestyle for individuals living in Switzerland.

Summary and Conclusions

References

Summary and Conclusions

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Summary and Conclusions

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